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Phototropism: Mechanism and Outcomes

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Plants have evolved a wide variety of responses that allow them to adapt to the variable environmental conditions in which they find themselves growing. One such response is the phototropic response - the bending of a plant organ toward (stems and leaves) or away from (roots) a directional blue light source. Phototropism is one of several photoresponses of plants that afford mechanisms to alter their growth and development to changes in light intensity, quality and direction. Over recent decades much has been learned about the genetic, molecular and cell biological components involved in sensing and responding to phototropic stimuli. Many of these advances have been made through the utilization of Arabidopsis as a model for phototropic studies. Here we discuss such advances, as well as studies in other plant species where appropriate to the discussion of work in Arabidopsis.

INTRODUCTION

Light, apart from being an essential source of energy for plants, also provides a multitude of cues for proper growth and development. Phototropism, or the directional curvature of organs in response to lateral differences in light intensity and/or quality, represents one of the most rapid and visually obvious of these responses (Darwin, 1880; Sachs, 1887; Iino, 1990). Although a number of plant organs appear to be responsive to phototropic stimuli (Iino, 1990; Koller, 1990), a vast majority of the experimental data related to phototropism deals with the responses observed in seedling stems and primary roots. In particular, stems have been shown to exhibit positive phototropism, or curvature towards the light (Figure 1), while roots show negative phototropism, or curvature away from the light. Stem phototropism is thought to provide plants with an effective means for increasing foraging potential (maximizing photosynthetic light capture) and is therefore likely to have appreciable adaptive significance (Iino, 1990; Stowe-Evans et al., 2001). Less is known about the phototropic response of roots, yet it is clear that cooperative interaction between a negative phototropic response and a positive gravitropic response could help to ensure proper growth of the root into the soil where water and nutrients are most abundant and available for absorption (Galen et al., 2004; Galen et al., 2007b). The adaptive advantage provided by stem and root phototropic responses may be particularly important during the early stages of growth and establishment of seedlings (Iino, 1990; Galen et al., 2004; Galen et al., 2007b) and during gap filling situations in dense canopy conditions (Ballare, 1999).

Phototropic responses are distinguished from other types of directional growth responses, such as nastic (Satter and Galston, 1981; Forterre et al., 2005) and circadian-regulated (McClung, 2001; Moshelion et al., 2002; Ueda and Nakamura, 2007) leaf movements, by two criteria. First, the direction of phototropic curvatures is determined by the direction of the light stimulus, while the directions of circadian-regulated movements are not (Salisbury and Ross, 1992). Second, many leaf movement responses occur as a result of reversible swelling/shrinking of specialized motor, or pulvinar, cells (Hart, 1988; Koller, 1990; Moran, 2007) whereas all stem and root phototropic responses are driven by changes in cell elongation rates across the bending organ. With respect to phototropic responses, unidirectional irradiation of seedlings with UV-A/blue light (BL) results in enhanced growth of the stem within the flank away from the light (“shaded side”) and generally represses growth in the flank facing the incident light (“lit side”) (Baskin et al., 1985; Briggs and Baskin, 1988; Orbovic and Poff, 1993; Esmon et al., 2006), causing it to bend towards the light (Iino, 1990). An essentially opposite response is observed in roots, where growth is enhanced in the “lit side” and repressed in the “shaded side”, causing the root to bend away from the light (Okada and Shimura, 1992; Kiss et al., 2002; Kiss et al., 2003b). The differential growth rates driving the development of phototropic curvatures appear to be established as a result of differential accumulation of (Went and Thimann, 1937), and subsequent responsiveness to, the plant hormone auxin (Went and Thimann, 1937; Iino, 1990; Liscum and Stowe-Evans, 2000; Esmon et al., 2006).

One feature shared between stem/root phototropic responses and nastic leaf movement responses is co-localization of photoperception and growth response, namely that the cells exhibiting the "growth response", however mechanistically different, are the same ones perceiving the light signals (Briggs, 1963b; Koller, 1990). This is not necessarily the case with either circadian-dependent or true phototropic movements of leaves, where cells in the leaf blade perceive the signal, and pulvinar cells at the base of the leaf or petiole exhibit the growth response (Schwartz and Koller, 1978; Engelmann and Johnsson, 1998; Moran, 2007). In nastic leaf movements the movements resulting from asymmetrical turgor pressure changes, also referred to as an "osmotic motor", are driven by plasma membrane ATPase affecting KCl flux and thus water movement, into or out off the cells. Light, circadian and exogenous mechanical signals are known to feed into this osmotic motor to regulate leaf movements (Moshelion et al., 2002; Moran, 2007).

"The Weed of Enlightenment"

The phototropic response has been utilized for over 100 years as a system for studying two basic cellular processes in plants - signal transduction and cell elongation. In the past couple of decades, significant leaps have been made in our understanding of the biochemical and molecular events mediating phototropism. Although not solely responsible for these advances, the utilization, since the mid 1980's, of Arabidopsis as a model organism for studies of phototropism has played an important role. In fact, it is fair to say that like many other aspects of plant biology, "we would not be where we are today without Arabidopsis." This chapter will attempt to summarize these advances, with attention being given to both mechanism (e.g., the photoreceptor molecules and signal-response elements associated with various components of phototropic responses) and outcome (e.g., ecological and evolutionary significance of phototropism). While most of the discussion presented here will revolve around studies in Arabidopsis, reference will be made to studies in other organisms where contextually or historically important. For a more broad perspective on phototropism the reader is referred to a number of other sources (Darwin, 1880; Sachs, 1887; Banbury, 1959; Thimann and Curry, 1961; Briggs, 1963b; Firn and Digby, 1980; Dennison, 1984; Hart, 1988; Iino, 1990; Firn, 1994; Whippo and Hangarter, 2006; Christie, 2007; Holland et al., 2009).

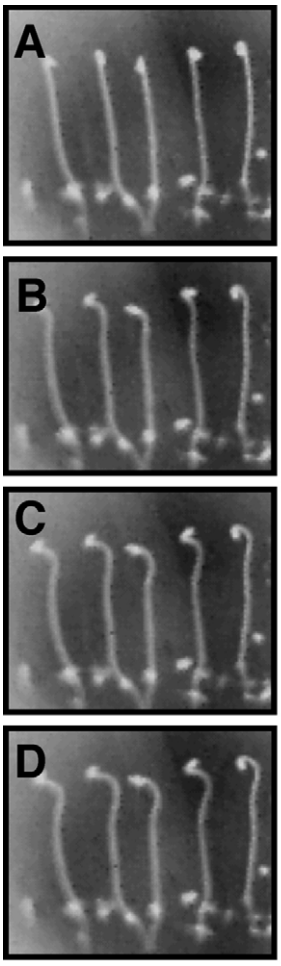

Figure 1. Phototropism in Arabidopsis induced by low fluence rate blue light. Photographs show 3-d-old etiolated seedlings 0 **(A)**, 100 **(B)**, 200 **(C)**, and 300 min **(D)** after the blue light was turned on. Incident light (coming from the left at a fluence rate of 0.002 μmol m^{-2} s^{-1}) was obtained from one blue light emitting diode (λ_{max} = 440 nm, 30 nm half-band). Note that the slight backwards bend in the upper hypocotyls region is an artifact that results from the seedlings being grown along an agar surface such that the cotyledons contain the positive phototropic response because they often lodge in the agar.

PERCEPTION OF DIRECTIONAL LIGHT CUES

Evidence for Two Distinct Blue-Light (BL) Photoreceptors for Phototropism: A Historical Perspective

Most studies of higher plant phototropism, including those with Arabidopsis, have been done using etiolated (dark-grown) seedlings and low fluence rate (< 0.5 μmol m^{-2} s^{-1}) BL (Dennison, 1984; Hart, 1988; Iino, 1990; Galland, 1992; Firn, 1994). Although the total fluence (number of photons per unit area; e.g., μmol m^{-2}) to which seedlings were exposed varied as much as six orders of magnitude from one experiment to the next, results from such studies suggested that a single photoreceptor mediates phototropic responsiveness under low fluence rate conditions (Poff et al., 1994; Liscum and Stowe-Evans, 2000). This conclusion holds independent of whether pulses (seconds or fractions of seconds) or extended irradiations (minutes to a few hours) are used. While the function of a single receptor over such a broad fluence response range might seem unlikely, similar broad fluence-responsive properties have long been recognized for the red (RL)/far-red (FR) light-absorbing phytochromes (phys) (Mancinelli, 1994).

In contrast to the single photoreceptor prediction from studies employing low fluence rate conditions, the function of at least two distinct photoreceptor molecules has been suggested for phototropic curvatures induced by high fluence rate BL (Konjevic et al., 1989b; Konjevic et al., 1989a). In an elegant series of studies

in Arabidopsis, Konjevic and colleagues (Konjevic et al., 1989a) obtained several pieces of physiological evidence in support of a two-receptor model. First, while irradiation with a single pulse of low fluence rate (e.g., 0.1 μmol m^{-2} s^{-1}) BL (450 nm) led to a single-peak biphasic fluence-response curve for phototropism (Figure 2A), use of higher fluence rate (e.g., 0.7 μmol m^{-2} s^{-1}) BL resulted in a clear dual-peak response curve (Figure 2B). Second, this curious alteration in fluence responsiveness was also dependent upon wavelength. For example, irradiation with 490 nm light resulted in a single peak fluence-response curve with a distinct lower-fluence shoulder (Figure 2C), while use of 510 nm light gave rise to only a single peak curve with no shoulder (Figure 2D). Such wavelength- and fluence rate-dependent changes in fluence-responsiveness are not expected for the action of a single photoreceptor. Third, the second higher-fluence peak of the 450 nm fluence-response curve (Figure 2B) could be eliminated by a pre-irradiation with a saturating pulse of 510 nm light (25 μmol m^{-2}), a unexpected phenomenon if a single receptor were responsible for both fluence-response peaks. Fourth, sequential irradiation with 510 and 450 nm light at a fluence and fluence rate that gives rise to maximal single-peak responses (Figure 2A and D), resulted in a phototropic response that was nearly additive. As discussed below the action of two photoreceptors in high fluence rate-induced phototropism has now been confirmed through molecular genetic studies in Arabidopsis, though all of the photophysiological properties described by Poff and colleagues have not been fully explained by the two identified receptors. While the genetic identification and basic biochemical properties of these photoreceptors will be addressed here, we refer the reader to other sources for more detailed discussion of these receptors and their roles in non-phototropic processes (Christie and Briggs, 2001; Celaya and Liscum, 2005; Stone et al., 2005; Briggs, 2007; Christie, 2007).

Phototropin 1 (phot1): A Broad Fluence Rate-Responsive Phototropic Receptor

The first significant progress towards the identification of an apoprotein for a low fluence rate phototropic receptor came in 1988 with a report of a BL-activated phosphorylation of a plasma membrane-localized protein in etiolated pea seedlings (Gallagher et al., 1988). As discussed in a review by Short and Briggs (Short and Briggs, 1994), the phosphorylation of a single plasma membrane protein (114 to 130 kDa, depending upon the species) appears to be a ubiquitous response of higher plants to BL irradiation. Many of the photophysiological properties of this light-dependent phosphorylation reaction, as determined in a number of species (most notably maize, oat, pea, and later Arabidopsis), suggested it was important for phototropic responses. For example, the phosphorylation reaction occurs in the most phototropically sensitive tissues, it is strongest in the tissue closest to the light and decreases in strength moving away from the lit side, it is fast enough to precede the development of curvature, its action spectrum matches that for phototropism, and it shows similar dark-recovery kinetics as phototropism after a saturating irradiation (Short and Briggs, 1994; Briggs and Huala, 1999).

A genetic connection between the aforementioned phosphorylation reaction and phototropism came in 1992, when Reymond and colleagues (Reymond et al., 1992b) showed that a phototropic mutant of Arabidopsis, strain JK224 (Khurana and Poff, 1989), exhibited little, if any, BL-induced phosphorylation. Strain JK224 was originally described as a mutant that exhibited a shift in its fluence threshold (10 to 30-fold higher) for pulse light-induced BL-dependent phototropism (Khurana and Poff, 1989). It was subsequently proposed, based on responsiveness to BL and green light (GL) at low and high fluence rates, that strain JK224 contains a lesion in a photoreceptor (Konjevic et al., 1992), in particular the low fluence rate receptor system described by Konjevic and colleagues (Konjevic et al., 1989a). Liscum and Briggs (Liscum and Briggs) demonstrated that null mutations in

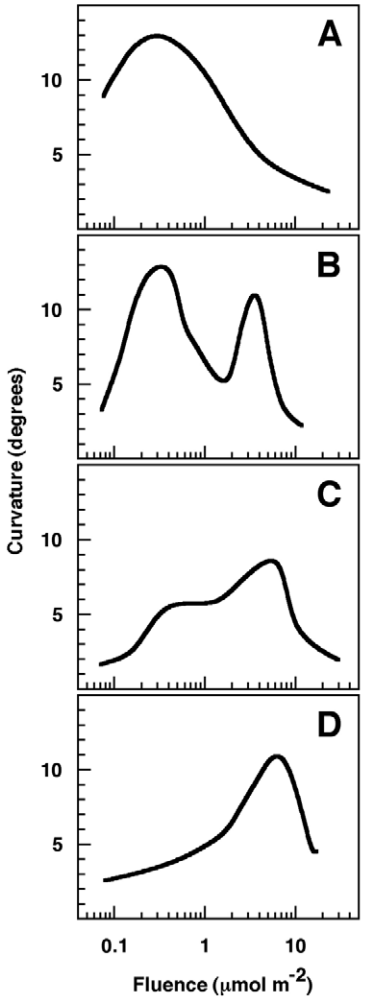

Figure 2. Fluence rate and wavelength dependence of pulsed light-induced phototropism in Arabidopsis (adapted from (Konjevic et al., 1989)

(A) Phototropism induced by a single pulse of blue light (λ_{max} = 450 nm, 10 nm half-band) at a "low" fluence rate (0.1 μmol m^{-2} s^{-1}).
(B) Phototropism induced by a single pulse of blue light (λ_{max} = 450 nm, 10 nm half-band) at a "high" fluence rate (0.7 μmol m^{-2} s^{-1}).
(C) Phototropism induced by a single pulse of blue/green light (λ_{max} = 490 nm, 10 nm half-band; at a fluence rate of 0.9 μmol m^{-2} s^{-1}).
(D) Phototropism induced by a single pulse of green light (λ_{max} = 510 nm, 10 nm half-band; at a fluence rate of 0.4 μmol m^{-2} s^{-1}).

the *NONPHOTOTROPIC HYPOCOTYL 1* (*NPH1*) locus, of which the mutation in strain JK224 is an allele (*nph1-2*), fail to show BL-dependent phosphorylation because they in fact lack the target protein. Hence, it was hypothesized that the *NPH1* locus encodes the apoprotein for a phototropic receptor and that the observed BL-induced phosphorylation represents an autophosphorylation response (Liscum and Briggs, 1995).

Cloning of the *NPH1* gene (Table 1) showed that the encoded protein is of the proper size (120 kD in Arabidopsis; (Reymond et al., 1992a)) to be the substrate of the phosphorylation reaction (Huala et al., 1997). The predicted NPH1 protein was also shown to contain the eleven signature domains of Ser/Thr protein kinases (Figure 3), making autophosphorylation a formal possibility. On the other hand, nothing was found in the primary sequence that indicated an obvious inherent photoreceptor activity for NPH1. However, a repeated sequence motif within the amino-terminal portion of NPH1 was identified (Figure 3) that exhibits homology to a subfamily of PAS domains that are found within sensor-proteins (Huala et al., 1997; Zhulin et al., 1997; Taylor and Zhulin, 1999). Both of these PAS-like domains of NPH1, designated LOV1 and LOV2 (for their relationship to light, oxygen, and voltage-regulated PAS domains), were subsequently shown to bind one FMN molecule (Christie et al., 1998), a finding consistent with the hypotheses that NPH1 represents a BL-absorbing phototropic receptor (Khurana and Poff, 1989; Konjevic et al., 1992; Liscum and Briggs, 1995). Soluble nph1 (NPH1 apoprotein with associated FMN cofactors; see Table 2 for nomenclature) isolated from a heterologous insect cell expression system was shown to exhibit BL-dependent autophosphorylation with kinetic, fluence-response, and action spectrum characteristics essentially like those obtained with native Arabidopsis nph1, and for phototropism itself (Christie et al., 1998). Hence, in the absence of all other plant proteins nph1 can function as a photoreceptive molecule with the properties consistent with its function as a phototropic receptor in plants.

As discussed above, genetic studies in Arabidopsis have demonstrated that nph1 is necessary for normal phototropic response to directional low fluence rate UV-A, BL, and GL, and it is presumed that the light-activation of nph1's kinase domain is critical to its signaling properties. Biochemical and structural studies suggest that the kinase domain of nph1 is activated in response to a light-dependent formation of a self-contained FMN- C(4a)-cysteinyl adduct (Salomon et al., 2000; Crosson and Moffat, 2001). The nph1 holoprotein has been given the trivial name, phototropin 1 (phot1), in order to reflect its physiological and biochemical properties (Christie et al., 1999; Briggs et al., 2001); see Tables 1 and 2).

A second phototropin gene, *PHOT2* (previously designated *NPL1*, for *NPH1-like*; see Tables 1 and 2), has been identified in the Arabidopsis genome (Jarillo et al., 1998; Initiative, 2000), and the function of its encoded protein as a second phototropic receptor will be discussed in the following section.

Phototropin 2 (phot2): A Second High Fluence Rate Phototropic Receptor

As discussed earlier, pulse-irradiation experiments suggested that two photoreceptors are capable of modulating response to directional BL, in a fluence rate-dependent fashion (Konjevic et al., 1989a; Konjevic et al., 1992). Additional physiological and genetic support for this two-photoreceptor hypothesis came from studies of etiolated *nph1* (*phot1*)-null mutants under long-term irradiation conditions (Liscum and Stowe-Evans, 2000; Sakai et al., 2000). For example, Sakai and colleagues (Sakai et al., 2000) found that while *phot1-101* lacks hypocotyl and root phototro-

Table 1. Genes shown to be definitively involved in phototropic signal perception, transduction, and response

Gene1	Synonym(s)[2]	AGI locus no.	Gene ID[3]	Phototropic function
ABCB19	*MDR1,PGP19*	At3g28660	822519	Regulation of auxin-transport
AXR1	*none*	At1g05180	839286	Regulation of auxin-response
NPH3	*RPT3*	At5g64330	836554	Signal transduction; phot1, RPT2 and PKS1 interacting protein
NPH4	*ARF7,BIP,MSG1,TIR5*	At5g20730	832196	Regulator of auxin-response
PHOT1	*JK224,NPH1*	At3g45780	823721	Primary photoreceptor
PHOT2	*CAV1,NPL1*	At5g58140	835926	Primary photoreceptor
PHYA	*FRE1,FHY2,HY8*	At1g09570	837483	Major secondary/modulatory photoreceptor
PHYB	*HY3*	At2g18790	816394	Minor secondary/modulatory photoreceptor
PIN1	*none*	At1g73590	843693	Relocalzation of auxin
PIN3	*none*	At1g70940	843432	Relocalization of auxin
PKS1	*none*	At2g02950	814823	Signal transduction; phot1, phyA, phyB and NPH3 interacting protein
RPT2	*none*	At2g30510	817601	Signal transduction; phot1 and NPH3 interacting protein

[1]Standard gene name established by the community or the one most commonly used in conjugation with a discussion of phototropism
[2]Additional names for the genes given in the first column. Citations for the first reference to the synonoymous gene are as follows: *RPT3* (Okada and Shimura, 1994); *BIP* (GenBank only, AAD04807); *MSG1* (Watahiki and Yamamoto, 1997); *TIR5* (Ruegger et al., 1997); *JK224* (Khurana and Poff, 1989); *NPH1* (Liscum and Briggs, 1995); *CAV1* (Kagawa et al., 2001); *NPL1* (Jarillo et al., 1998); *FRE1* (Nagatani et al., 1993); *FHY2* (Whitelam et al., 1993); *HY8* (Parks and Quail, 1993); *HY3* (Koornneef et al., 1980). *MDR1* (Noh et al., 2001).
[3]Gene ID number as recorded in NCBI Entrez Gene register (Maglott et al., 2007).

pism at fluence rates < 1.0 µmol m^{-2} s^{-1}, it retains a phototropic response at fluence rates of BL above ~1.0 µmol m^{-2} s^{-1} and is essentially like wild-type at 100 µmol m^{-2} s^{-1}. Similar results have been observed with the *phot1-5* null mutant under greenhouse conditions (T. Campbell and E. Liscum, unpublished). Thus, while there is ample genetic, biochemical, and physiological evidence to conclude that phot1 is a phototropic receptor under low fluence rate (< 1.0 µmol m^{-2} s^{-1}) conditions (Liscum and Stowe-Evans, 2000), the aforementioned results clearly indicate that a second phototropic receptor functions under high fluence rate (1 µmol m^{-2} s^{-1}) conditions (Table 2).

The most obvious candidate for a second phototropic receptor apoprotein is the PHOT1 paralog PHOT2 (Jarillo et al., 1998). Although PHOT2 is slightly smaller than PHOT1 (110 kD versus 124 kD), sequence and structural motifs are highly conserved. In particular, PHOT2, like PHOT1, contains a Ser/Thr protein kinase domain in its carboxyl terminal region and two LOV domains in its amino terminal half (Jarillo et al., 1998); (Figure 3). Moreover, the light-dependent autophosphorylation and photocycling properties of baculovirus/insect cell-expressed phot2 are similar to those of phot1 (Sakai et al., 2001), suggesting that phot2 functions as a BL receptor by a mechanism analogous to that of phot1.

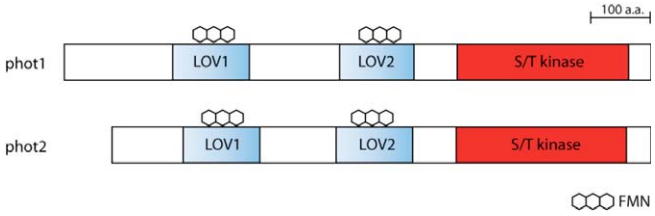

Figure 3. Domain structures of the phot1 and phot2 receptors. The amino-terminal photosensory LOV domains are shown in blue with their associated FMN co-factor (above each LOV domain). The carboxyl-terminal protein kinase domain of each phot is shown in red.

Table 2. phototropin nomenclature[1]

Wild type genes	*PHOT1,PHOT2*
Mutant genes	*phot1, phot2*
Apoprotein[2]	PHOT1, PHOT2
Holoprotein[2]	phot1, phot2

[1]The nomenclature for the phototropins presented here has recently been described by Briggs et. al. (2001) and is based upon the nomenclature adopted for the phytochromes (Quail et al., 1994). *PHOT1* was originally designated NPH1 (mutant=*nph*, for non-phototropic hypocotyl) (Liscum and Briggs, 1995), and *PHOT2* was originally designated NPL1 (NPH1-Like) (Jarillo et al., 1998).
[2]Phototropin apoproteins and holoproteins differ only in that holoprotein have associated with them the two flavin mononucleotide chromophores, while apoproteins lack these co-factors. As such the holoproteins are the "photoactive" entity.

While no alterations in phototropic responsiveness have been observed in phot2 single mutants (Sakai et al., 2000; Jarillo et al., 2001; Sakai et al., 2001), *phot1phot2* double mutants fail to exhibit seedling phototropic responses at both low and high fluence rates (Sakai et al., 2001). The fact that *phot2* single mutants retain a phototropic response indistinguishable from wild-type under all fluence rates tested (Jarillo et al., 2001; Sakai et al., 2001) while the *phot1phot2* double mutant is essentially blind (Sakai et al., 2001), demonstrates that phot1 functions to some extent under all fluence rate conditions, while phot2 has redundant function for phot1 specifically under high fluence rate conditions (Table 3). If the phot1 and phot2 holoproteins have similar photochemical and biochemical properties, as cited above, how can we explain these overlapping yet distinct functions in the perception of phototropic stimuli?

In a study by Aihara and coworkers (Aihara et al., 2008), chimeric proteins were constructed between amino-terminal LOV domains and with the carboxy-terminal kinase domains of both phot1 and phot2 to understand the fluence rate-dependent sensitivities of these photoreceptors. Chimeric proteins containing the combination of phot1 LOV domains with the protein kinase domain of phot2 were as sensitive as phot1 indicating that fluence rate sensitivity of a phototropin resides in the amino-terminal photosensory LOV domains. Moreover, combination of LOV domains of phot2 with the protein kinase domain of phot1 was less sensitive, akin to phot2. However, both these chimeras were able to promote chloroplast avoidance response that is specific to phot2 suggesting that the fluence sensitivity is more complex for other phototropin-dependent responses (Aihara et al., 2008).

Beyond the structural-functional divergences between phot1 and phot2, simple differences in expression patterns of the two genes/proteins likely also contribute to the conditional differences in functions of the two receptors. It is clear that steady-state levels of *PHOT1* and *PHOT2* mRNAs exhibit light-dependent differences (Table 3). While the abundance of *PHOT1* mRNA does appear to be under the control of the circadian oscillator – with highest levels being observed at midday (Harmer et al., 2000), acute light-dependent regulation of *PHOT1* expression has not

Table 3. Role of phototropins and associated signaling components in mediating responses in Arabidopsis

	phototropism	Stomatal opening	Chloroplast accumulation	Chloroplast avoidance	Leaf expansion	Leaf positioning	Leaf movement	Hypocotyl inhibition	mRNA stability
phot1	+	+	+	-	+	+	+	+	+
phot2	+	+	+	+	+	-	+	-	-
NPH3	+	-	-	-	-	+	-	-	+
RPT2	+	+	-	-	-	-	-	-	-
PKS1	+	-	-	-	-	-	-	+[1]	-

'+' indicates based on published results; '- ' based on published results or currently the role is unknown.
[1]PKS family member PKS4 mediates this response (Schepens et al., 2008).

been observed. In contrast, *PHOT2* mRNA levels increase upon exposure to UV-A, BL, RL, or white light (Jarillo et al., 2001; Sakai et al., 2001), apparently through the action of phyA (Tepperman et al., 2001). Strikingly, a two-fold increase in *PHOT2* steady-state message levels was observed at fluence rates of BL (~10 µmol m^{-2} s^{-1}) where the redundant function of phot2 is most obvious (Sakai et al., 2001). Light-dependent increase in *PHOT2* message level may, in addition to structural-functional differences between the two phototropin proteins, contribute to the high fluence rate-specific phototropic function of phot2. It is also worth noting that a more rapid dark-recovery time required by phot2, which is more than 10 times faster than that of phot1 (Kasahara et al., 2002; Kagawa et al., 2004), has also been proposed as a contributor to the higher fluence-rate threshold for phot2 activity (Sakai et al., 2001; Takemiya et al., 2005).

LOV Domain Functionality

Independent of exactly how different fluence rate dependencies for phot1 and phot2 responses arise, the protein kinase domain of phot2 alone has been found to be sufficient to trigger constitutive light-independent phot2 specific responses, such as stomatal opening and the chloroplast avoidance response (Kong et al., 2007). This would prompt one to ask the question, what role do LOV photosensory domains play in photoperception? It has been demonstrated that the LOV2 domain regulates the protein kinase activity of phot2 *in vitro* (Matsuoka and Tokutomi, 2005), and that LOV2 photoactivity is required for *in vivo* autophosphorylation of phot1 and subsequent phototropism in response to BL exposure (Christie et al., 2002; Cho et al., 2007). Similarly, the LOV2 domain is sufficient to stimulate phot2 protein kinase activity for phototropism in Arabidopsis (Cho et al., 2007) and for chloroplast movement in *Adiantum* (Kagawa et al., 2004). LOV1 alone is unable to stimulate autophosphorylation of phot1 in response to BL, or to promote phototropism, suggesting that the LOV2 domain plays a major role in photoperception and subsequent activation of the protein kinase domain to promote phototropism (Christie et al., 2002; Harper et al., 2003; Cho et al., 2007).

At this juncture, a precise role played by LOV1 domain is not entirely clear. While LOV1 undergoes an FMN-dependent photocycle like that of LOV2 (Kasahara et al., 2002; Christie, 2007), it has been reported that LOV1 may promote dimerization of the phots. This proposal is based on studies of amino-terminal *Avena sativa* phot1 polypeptides expressed in *E. coli* and studied in solution via gel-chromatography (Salomon et al., 2004). X-ray crystallographic studies on the LOV1 domain of phot1 and phot2 also support the homo-dimerization thesis (Nakasako et al., 2008). In this latter study the authors reported that homodimers were formed *in crystal* through face-to-face association of the beta-sheets of respective LOV1 domains. Surprisingly, the critical residues apparently mediating dimerization of LOV1 domains differ between phot1 and phot2 (Nakasako et al., 2008). Although further studies are required to determine if full-length phototropins are capable of forming dimers *in planta*, a recent study demonstrated that a fully active version of phot1 can transphosphorylate a kinase-dead version of phot1 in planta, suggesting that homodimerization is likely (Kaiserli et al., 2009). Heterodimerization between phot1 and phot2 also cannot be ruled out at this moment as phot2 is capable of cross-phosphorylating kinase-dead phot1 mutant *in vitro* (Cho et al., 2007).

Light-Dependent Intracellular Relocalization of phot1 and phot2: Receptor Desensitization, Foundation for Phototropic Signaling, or Both?

Although phot1 and phot2 holoproteins lack obvious plasma membrane targeting signals or post-translational lipid/fatty-acids modification signatures, both are associated with the plasma membrane, as observed in various plant species (Christie et al., 1998; Sakamoto and Briggs, 2002; Knieb et al., 2004; Kong et al., 2006; Zienkiewicz et al., 2008). While the exact mechanism by which phototropins are associated with the plasma membrane remains unknown, ionic interactions are not likely the basis as extensive washing of microsomal membranes with high salt buffer fails to release phot1 into solution (Knieb et al., 2004). Recent serial-deletion analyses in Arabidopsis have however demonstrated that the protein kinase domain of phot2 is sufficient for its plasma membrane localization (Kong et al., 2006; Kong et al., 2007).

A study by Sakamoto and Briggs (Sakamoto and Briggs, 2002) observed movement of a phot1-GFP fusion protein from plasma membrane into the cytosol upon BL irradiation. Consistent with these observations, appreciable amounts of phot1 protein have been detected by immunoblot analysis in soluble protein fractions prepared from *in vivo* BL irradiated Arabidopsis seedlings (Sakamoto and Briggs, 2002; Knieb et al., 2004). Downregulation of phot1 protein levels were also observed after prolonged treatment with BL, in a fluence and time dependent manner (Sakamoto and Briggs, 2002; Kong et al., 2006). It has been estimated that in etiolated mustard seedlings upon BL irradiation, cytoplasmic phot1 ($[phot1]_{cyt}$) constitutes approximately 20% of the total cellular phot1 (Knieb et al., 2004). It is currently unknown whether $[phot1]_{cyt}$ is part of an endosomal vesicle or other sub-cellular component (Sakamoto and Briggs, 2002; Wan et al., 2008). Treatment of seedlings with protein synthesis inhibitor cycloheximide fails to disrupt the production of $[phot1]_{cyt}$, indicating that $[phot1]_{cyt}$ is derived *de novo* from the plasma membrane associated phot1 (Wan et al., 2008). Moreover, it has recently been shown that phot1 movement from the plasma membrane apparently represents a clathrin-dependent endocytosis event (Kaiserli et al., 2009). Though $[phot1]_{cyt}$ disappears gradually over time, it is presently unclear whether it cycles back to the plasma membrane or undergoes degradation.

Unexpectedly, upon BL treatment phot2 translocates from the plasma membrane to cytoplasmic vesicles which co-localize with a Golgi marker K.AM1/MUR3 in Arabidopsis (Kong et al., 2006). In contrast to phot1, no phot2 was detected in soluble proteins extracts prepared from *in vivo* BL irradiated seedlings, nor did total phot2 protein levels change appreciably (Kong et al., 2006). It is intriguing to note that in spite of having similar overlapping photosensory function in phototropism and other responses, phot1 and phot2 relocalize to apparently distinct cellular compartments in response to BL (Kong et al., 2006; Kong et al., 2007).

What is the functional role of BL induced relocalization of phots? It has been hypothesized that relocalization of phots modulates their activity (Kong et al., 2006; Wan et al., 2008). It is attractive to speculate that different sub-cellular localizations of

a phot might elicit different responses. In this context it is worth noting that in guard cells, $[phot1]_{cyt}$ was not detected, indicating that phot1 movement does not occur in all cell types, and is not prerequisite for all responses (Wan et al., 2008). In addition, Kong and colleagues (Kong et al., 2006) have shown that phot2 is able to mediate chloroplast movement in cells treated with brefeldin A (BFA), an inhibitor of vesicular endomembrane recycling (Nebenführ et al., 2002). This latter observation indicates that presumed vesicular trafficking of phot2 to Golgi is not required for chloroplast movement responses (Kong et al., 2006). Yet, a potential signaling role of phots from internalized membrane vesicles should probably not be discounted offhand since such potential vesicle-based signaling mechanisms are not unknown in plants. For example, BRI1 (BRASSINOSTEROID INSENSITIVE 1), the brassinosteroid hormone receptor-like kinase (Wang et al., 2006), localizes to both the plasma membrane and endosomes, and enhancement of brassinosteroid signaling is observed after treatment with BFA, suggesting that signaling occurs from endosomal-localized BRI1 (Geldner et al., 2007).

If the active site of phot signaling were to be exclusively at the plasma membrane rather than some internalized compartment, what then is the role of phot relocalization from the plasma membrane to cytoplasmic locations? One obvious possibility is that such internalization could serve to attenuate signaling by removing the receptor from the site of action. Such a mechanism is not uncommon in mammals, where cell surface and plasma membrane-associated receptors are regularly internalized by various mechanisms to desensitize receptor activity (Vieira et al., 1996; von Zastrow and Sorkin, 2007). Various receptor internalization pathways have been documented, and of them clathrin-dependent receptor endocytosis is by far the most well studied (Holstein, 2002), making the findings of Kaiserli and colleagues that phot1 is apparently endocytosed in a clathrin-dependent fashion (Kaiserli et al., 2009) particularly intriguing. Many receptors, upon binding their respective ligand, trigger their own internalization to modulate signaling (Mellman, 1996). An example of such a mechanism in plants is the receptor-like kinase FLAGELLIN-SENSING 2 (FLS2). Upon binding of its ligand, flagellin or its derivative flg22 peptide, FLS2 undergoes ligand-mediated endocytosis (Robatzek et al., 2006). It thus seems plausible that a phot, upon perceiving its ligand – BL, could induce its own internalization to reduce the number of signal-active receptors present on the plasma membrane, thus desensitizing the overall cellular responsiveness to light. It is intriguing to note phyA activation with RL can inhibit the BL-induced movement of phot1 from the plasma membrane (Han et al., 2008). These results are consistent with phot1 functioning at the plasma membrane and internalization representing a desensitization process since RL absorbed by phyA is known to result in enhanced phototropic responsiveness (Parks et al., 1996; Janoudi et al., 1997b; Stowe-Evans et al., 2001; Whippo and Hangarter, 2004). The influences of phyA on the modulation of phototropism will be discussed in detail later.

Are There Additional Directional Light Sensors?

As discussed above and later, there is overwhelming evidence to conclude that phot1 and phot2 are phototropic receptors. However, in plants, twelve photoreceptors are known to exist in addition to phot1 and phot2 - five phys, three cryptochromes (crys), one chimeric phot/phy called neochrome (*Adiantum* PHY3) and three ZEITLUPE/ADAGIO (ZTL/ADO) family members (Briggs and Olney, 2001; Chen et al., 2004; Banerjee and Batschauer, 2005; Franklin et al., 2005; Lin and Todo, 2005; Wang, 2005; Christie, 2007). The ZTL/ADO proteins have been shown to participate in BL-dependent targeting of components of the circadian clock for ubiquitylation and proteasomal degradation (Imaizumi et al., 2003; Banerjee and Batschauer, 2005; Briggs, 2007; Christie, 2007; Kim et al., 2007; Sawa et al., 2007). Three members of the ZTL/ADO family have been identified in Arabidopsis: ZTL/ADO (Somers et al., 2000); FLAVIN-BINDING, KELCH REPEAT, F-BOX (FKF1) (FKF1; Nelson et al., 2000); and LOV KELCH REPEAT PROTEIN 2 (LKP2) (LKP2; Schultz et al., 2001). Each of the ZTL/ADO family members contains a single LOV domain that utilizes FMN as its BL-absorbing chromophore. Moreover, it appears that the photocycle of ZTL/ADO LOV domain-FMN interactions is conserved with that of the phots (Imaizumi et al., 2003; Kim et al., 2007; Sawa et al., 2007). The wide selection of photoreceptors available to plants poses the question of whether any of these, apart from phot 1 and phot 2, function as primary receptors of directional BL cues? In etiolated seedlings the short answer to this question is apparently no. However, to be fair the potential role(s) of the phot-related ZTL/ADO proteins in phototropism has yet to be extensively examined.

Crys Appear Not to Function as Directional Sensors

In 1998, Ahmad and colleagues proposed that the cry BL receptors, cry1 and cry2 (Batschauer, 1999; Briggs and Huala, 1999; Cashmore et al., 1999; Christie and Briggs, 2001), represent redundant primary phototropic receptors in etiolated Arabidopsis seedlings (Ahmad et al., 1998b). This conclusion was based upon the observations that while *cry1* and *cry2* single mutants (containing equivalent G to E substitutions within the FAD-binding domain) retained a normal phototropic response, the *cry1cry2* double mutant lacked response, and cry1 and cry2 overexpressing lines were hypersensitive to unilateral BL. Moreover, it was suggested that cry1 and cry2 function upstream of phot1 in phototropic signaling since BL-dependent autophosphorylation of phot1 appeared impaired in the *cry1cry2* double mutant.

A subsequent study by Lascève and colleagues (Lascève et al., 1999) found that two independent *cry1cry2* double mutant lines (*hy4-B104cry2-1* and *cry1-304cry2-1*) which lack detectable cry1 and cry2 proteins altogether (Guo et al., 1998; Mockler et al., 1999) retained both BL-induced phototropism and phot1 autophosphorylation – in stark contrast to the results obtained for the substitution mutants in the study by Ahmad and colleagues (Ahmad et al., 1998b). Although a slight reduction in the magnitude of maximal pulse-induced phototropism was observed in the *cry1cry2* double mutants, no change in the threshold or peak-response fluence dependencies was observed (Lascève et al., 1999). In contrast, the *phot1-2* mutant (originally designated strain JK224) retains a phototropic response of equal magnitude to wild-type, but exhibits a 20 to 30-fold shift in fluence responsiveness (Khurana and Poff, 1989; Konjevic et al., 1992), as would be expected for a photoreceptor mutant that retains a response. Lascève and colleagues concluded that neither cry1 nor cry2 function

as primary phototropic receptors, or as photoreceptors that mediate BL-induced phosphorylation of phot1. A subsequent study of phototropism in *phot1, phot2, cry1* and *cry2*, as single and multiple mutants, at fluence rates of BL ≤100 μmol m^{-2} s^{-1}, provided additional support for the conclusion that the only primary phototropic photoreceptors are the phototropins (Ohgishi et al., 2004).

Based on results from a study employing a sensitive mathematical approach to measure phototropic curvatures from time-lapse images of etiolated Arabidopsis seedlings exposed to unidirectional BL, Whippo and Hangarter proposed that proper phototropism represents a balance between the differential growth response induced by phot action and the hypocotyl growth inhibition response mediated by crys in a fluence rate-dependent fashion (Whippo and Hangarter, 2003). Recently it has been reported that crys have a negative effect on the phot1 transcript and protein accumulation in light grown seedlings when compared with etiolated seedlings (Kang et al., 2008), which could provide a more direct connection between the two pathways. While it is quite clear that crys do not act as primary phototropic receptors, future studies will be required to determine how much influence crys are having on phototropism via general effects (e.g., growth inhibition) *versus* those on phot signal-response more directly (e.g., modulation of phot1 protein levels).

Phys Appear to Sense Directional R/FR Cues and Contribute to Phototropism in De-etiolated But Not Etiolated Plants

Even before the molecular identification of the phots, the phytochrome (phy) family of RL/FR receptors (Casal, 2000; Fankhauser, 2001; Bae and Choi, 2008) had been proposed to function as mediators of phototropic responses in de-etiolated (light-grown) seedlings of a number of species (Atkins, 1936; Shuttleworth and Black, 1977; Ballare et al., 1992). As one example, cucumber seedlings exhibit phyB-dependent negative phototropism in response to perception of FR reflected from canopy plants (Ballare et al., 1992; Ballare et al., 1995). Pretreatment of etiolated seedlings with RL prior to phototropic stimulation with unilateral BL is known to modulate phototropic responsiveness (Briggs, 1963a; Chon and Briggs, 1966; Stowe-Evans et al., 2001). RL-induced enhancement of hypocotyl phototropism under low fluence rate BL conditions (0.01 μmol m^{-2} s^{-1}) appears to be controlled primarily by phyA, whereas phyB and phyD redundantly influence phototropism at higher fluence rates of BL (e.g., 1.0 μmol m^{-2} s^{-1}) (Whippo and Hangarter, 2004). Interestingly, RL promotes positive phototropism in Arabidopsis roots, while BL promotes negative root phototropism (Ruppel et al., 2001; Esmon et al., 2005). The positive root phototropic response to RL is not very apparent, as it is significantly weaker than BL-dependent negative phototropism and strong gravitropic responses. By employing mutants defective in gravitropism it has been demonstrated that phyA and phyB promote positive phototropism in roots (Kiss et al., 2003a). It is however unclear at this time precisely how phys are sensing directional light cues to promote photo-movements.

Despite their influences on positive root phototropism, experimental evidence argues against a role for a phy as a primary receptor of directional BL cues in hypocotyls of etiolated Arabidopsis seedlings. First, RL (or FR) does not induce shoot phototropism in etiolated seedlings of most species, including Arabidopsis (Steinitz et al., 1985; Liscum and Briggs, 1996). Because phy function is coupled to its photocycling between the Pr (RL-absorbing) and Pfr (FR-absorbing) forms which can occur in response to irradiation with RL/FR or UV-A/BL (Shinomura et al., 2000; Fankhauser, 2001), it is unlikely that phy can function as a primary phototropic receptor in BL if it is not doing so in RL or FR. Second, while the magnitude of phototropism is reduced in *phyA* and *phyB* mutants, the fluence dependencies of the responses are unchanged (Parks et al., 1996; Janoudi et al., 1997a; Janoudi et al., 1997b; Lascève et al., 1999), indicating that phyA and phyB are not likely to function as primary phototropic receptors. Thus, phys, like the crys, have been proposed to act as modulators of phot1/phot2-dependent phototropic responses (Liscum and Stowe-Evans, 2000; Stowe-Evans et al., 2001; Whippo and Hangarter, 2004). This modulatory activity will be discussed later in more detail.

Chloroplastic Zeaxanthin as a Phototropic Sensor: Enigma or Red Herring?

Historically there has been considerable debate over the identity of the chromophore mediating absorption of UV-A and BL cues, with two camps split between flavins and carotenoids (Shropshire, 1908; Galston, 1977; DeFabo, 1980; Briggs and Iino, 1983; Quinlones and Zeiger, 1994; Palmer et al., 1996; Quinones et al., 1996; Lascève et al., 1999). With the identification and characterization of the phots, which are clearly flavin-binding proteins capable of mediating primary perception of direction UV-A, BL, and GL cues in Arabidopsis, one would think the controversy over "flavins versus carotenoids" with respect to phototropism would be over. Not quite! In 2001, Jin and colleagues (Jin et al., 2001) found that hypocotyl phototropism in Arabidopsis appears to require mature chloroplasts and suggested the need for a functional xanthophyll cycle. Much of their conclusions are based upon a simple observation that mature chloroplasts are present within the bending region of the hypocotyl, and that RL pretreatments that increase BL-dependent phototropism also broaden the "zone of chloroplast maturation" within the hypocotyl.

While a causal relationship between chloroplast maturation and phototropism is impossible to derive from these correlative phenotypic data, the authors provided preliminary genetic evidence to support their hypothesis. First, the phytoene-accumulating *pds2* mutant that lacks all derivative carotenoid pigments (Norris et al., 1995) exhibited neither chlorophyll autofluorescence associated with mature functional chloroplasts, nor detectable hypocotyl phototropism. Second, a previously uncharacterized mutant designated *star*, that apparently exhibits delayed greening, failed to exhibit either phototropism or autofluorescent chloroplasts after a 2 hr exposure to low fluence rate unilateral BL (0.3 μmol m^{-2} s^{-1}), but exhibited both responses if pretreated with 4 hr of RL (4 μmol m^{-2} s^{-1}) prior to BL exposure. The story is not likely to end here however since wild-type Arabidopsis seedlings grown on norflurazon (an inhibitor of phytoene desaturase; (Bartels and McCullough, 1972; Britton, 1979), while exhibiting a dampened response, retain normal phototropic sensitivity (Orbovic and Poff, 1991). Norflurazon-treated seedlings phenocopy the chloroplast but not the phototropic defects of the *pds2*, similar to what has been observed for maize seedlings deficient in phytoene desaturase activity (Palmer et al., 1996).

What's the next chapter in this saga? While nearly overwhelming evidence indicates that carotenoids are not primary receptors of phototropic stimuli, it is equally clear that carotenoid deficiency reduces the magnitude of phototropic curvatures. One plausible explanation for these observations that is also consistent with the apparent relationship between chloroplast development and phototropism is that some function(s) of the chloroplast is important for full phototropic competence, directly or indirectly, and that carotenoid deficiency simply impairs normal chloroplast development/function. Although this particular hypothesis has not been tested, it is interesting to note that the biosynthesis of the phytochromobilin (PϕB), the phy chromophore, is entirely plastid localized (Terry et al., 1993; Kohchi et al., 2001), and that the activity of PϕB synthase, which converts biliverdin to PϕB (Kohchi et al., 2001), is stimulated by light in intact plastids, likely through production of NADPH (and ATP) via photosynthetic activity (Terry and Lagarias, 1991). Phys, as already mentioned and to be discussed later in detail, appear to modulate the output(s) from the phot-dependent pathways that lead to phototropism in etiolated Arabidopsis seedlings. Hence, if PϕB is limiting in etiolated seedlings, as appears to be the case at least in the hook region (Murphy and Lagarias, 1997), and its plastid-localized synthesis is directly related to the amounts of active holophy (apophy plus PϕB), defective chloroplast function might depress phototropic responses through reductions in the levels of photoactive phys that are capable of enhancing phot-mediated signaling. At this point it is important to keep an open mind relative to the role of the chloroplast and/or carotenoids in phototropism, and to develop new strategies to ask more directed questions like the one just proposed.

PHOTOTROPIC SIGNALING COMPONENTS

Phosphorylation: An Output Signal From Phots, A Cue for Sensor Adaptation, Both, or Neither?

As discussed above, the only photoreceptors that can clearly be assigned a role in primary perception of phototropic stimuli associated with etiolated seedling responses are phot1 and phot2 (Liscum and Briggs, 1995; Christie et al., 1998; Sakai et al., 2001). Given that both phot1 and phot2 are light-activated Ser/Thr protein kinases (Christie et al., 1998; Sakai et al., 2001; Matsuoka and Tokutomi, 2005) it is quite reasonable to hypothesize that phototropic signal transduction might involve phot-activated phosphorelays (Briggs and Huala, 1999; Fankhauser and Chory, 1999; Liscum and Stowe-Evans, 2000; Briggs and Olney, 2001; Christie and Briggs, 2001). If this hypothesis is correct the phots might be expected to associate with protein kinases or phosphatases; however, no such interactions have yet been described. In fact the only known *in planta* phosphorylation substrates for the phots are the phots themselves, with autophosphorylation being described for both phot1 (Christie et al., 1998) and phot2 (Sakai et al., 2001). However, the phot2 protein kinase domain has the ability to phosphorylate casein *in vitro* (Matsuoka and Tokutomi, 2005).

While the role of phot autophosphorylation is not entirely understood, at least one property of the reaction in maize, oat, and Arabidopsis indicates that the bulk of the phosphorylation of phot1 is not required for the induction of phototropism. Specifically, the fluence thresholds for low fluence rate-induced phototropism and bulk autophosphorylation differ by several orders of magnitude – phototropism being 2–3 orders more sensitive to BL than the autophosphorylation response (Palmer et al., 1993; Salomon et al., 1997; Christie et al., 1998). Generation of a protein kinase dead mutant of phot1, through substitution of Asp^{806} with Asn within the kinase domain that prevents binding of Mg^{2+} for phosphate transfer (Hanks and Hunter, 1995), results in the complete abolition of phot1 autophosphorylation and mediated responses (Christie et al., 2002; Inoue et al., 2008). This finding indicates that phot1 protein kinase activity is absolutely required for both autophosphorylation and subsequent phot1-dependent responses, although how the two are connected remains unknown. One possibility may be reflected by the hierarchical nature of the autophosphorylation response, where some sites exhibit BL-induced phosphorylation at lower fluences than others (Salomon et al., 2003). Thus it is plausible that while bulk phosphorylation may not be necessary for phototropism, phosphorylation at specific sites under lower fluence conditions may be prerequisite for phototropic signal transduction.

Additional insights have been made on phot1 autophosphorylation by comparison of phot1 phosphorylation sites between dark and *in vivo* BL-irradiated seedlings using gas chromatography-mass spectrometric techniques (Inoue et al., 2008; Sullivan et al., 2008). Multiple Ser and Thr phosphorylation sites have been identified throughout the phot1 polypeptide and among them Ser^{851} in the activation loop of phot1 kinase domain appears to be important for both proper phot1 localization (Kaiserli et al., 2009) and various phot1-mediated responses. For example, transgenic Arabidopsis seedlings carrying a Ser^{851} to Ala substitution fail to exhibit normal BL-induced phototropic, stomatal opening or chloroplast accumulation responses (Inoue et al., 2008). However, substitution of other phosphorylatable Ser residues with Ala, such as Ser^{849} in the activation loop, had little or no effect on phototropism (Inoue et al., 2008), suggesting that different sites have different biochemical roles in the modulation of phot activity. At present it is not known whether Ser^{851} represents a low or high fluence-responsive site as the corresponding site was not identified in the oat study discussed above (Salomon et al., 2003).

PROTEINS INVOLVED IN EARLY POST-PERCEOPTION SIGNALING

NPH3: A Modular Adaptor Protein and Regulator of phot Signaling

Despite extensive screening for loss-of-function phototropism mutants, only one mutant locus, *nph3*, has been described that appears to alter a protein that functions close to, but downstream of, the phot1 photoperception event (Liscum and Briggs, 1995, 1996; Motchoulski and Liscum, 1999). In particular, *nph3* mutations have been shown to disrupt phototropism in etiolated seedlings under low fluence rate conditions (<1 μmol m^{-2} s^{-1}) (Liscum and Briggs, 1996; Motchoulski and Liscum, 1999), as well as high fluence conditions (>1 μmol m^{-2} s^{-1}) (Inada et al., 2004) without affecting BL-induced autophosphorylation of phot1 (Liscum and

Briggs, 1995). By means of combinatorial mutant analysis NPH3 has been demonstrated to function in both phot1 and phot2 phototropic signaling (Inada et al., 2004).

The *NPH3* gene (Table 1) was isolated by a map-based cloning approach and found to encode a member of a novel family of plant-specific proteins (Motchoulski and Liscum, 1999). Not surprisingly, given the similarity of phenotypes and the genetic interaction between *phot* and *nph3* mutants, the *NPH3* transcript is expressed highly in dark-grown seedlings in all the tissues and remains unaffected by light (A. Motchoulski and E. Liscum, unpublished; (Inada et al., 2004), similar to what was discussed already for *PHOT1*. In rice, *COLEOPTILE PHOTOTROPISM1 (CPT1)*, was identified as an ortholog of *NPH3*, and *nph3* and *cpt1* mutants were found to have similar phenotypes implying that NPH3 and its orthologs have conserved functional roles across plant taxa (Haga et al., 2005).

As shown in Figure 4B, NPH3 belongs to a 33-member protein family in Arabidopsis, designated NRL (NPH3/RPT2-Like) after the founding members of the family – NPH3 (Motchoulski and Liscum, 1999) and ROOT PHOTOTROPISM 2 (RPT2) (Sakai et al., 2000). Primary amino acid sequence conservation between members of the NRL protein family is found in five discrete, positionally conserved, regions designated DIa, DIb, DII, DIII, and DIV (Figure 4A). Within domain DIV there is a consensus metazoan Tyr phosphorylation site ([RK]-x(2,3)-[DE]-x(2,3)-Y; (Patschinsky et al., 1982) that is conserved in 29 of the 33 members of the family, including NPH3 (RTCDDGLY^{545}) (Motchoulski and Liscum, 1999). Although it is not known whether phosphorylation can occur on Tyr^{545} of NPH3, it is worth noting that the *nph3-2* mutant that carries in an in-frame deletion of this residue is phenotypically indistinguishable from a null mutant (*nph3-6*) that contains a stop codon at the Trp^{2} position (Motchoulski and Liscum, 1999). It remains to be determined whether Tyr^{545} is important for function of NPH3 (e.g., is it differentially phosphorylated in 'signaling' and 'non-signaling' NPH3 isoforms?) or as a structural motif that regulates protein stability/abundance.

At present no general functional role for various members of NRL family in plants is easily predictable. Yet, recent reports by various groups suggest that the physiological roles played by various NRL members may be quite diverse. First, mutations of *NRL20*, known as *mab4/enp/npy1 (macchi-bou4/enhancer of pinoid/naked pins in yuc mutants1),* were isolated separately as enhancers of *pinoid* (*pid*) and *yucca* (*yuc*) phenotypes (Cheng et al., 2007; Furutani et al., 2007). Interestingly PID is a protein kinase whose catalytic domain clusters in the same phylogenetic clade as the phot kinase catalytic domain (Christensen et al., 2000; Benjamins et al., 2001; Galvan-Ampudia and Offringa, 2007). Moreover, PID appears to regulate the activity/function of PIN-FORMED (PIN) proteins, a class of auxin efflux carriers, to modulate asymmetric and polar auxin transport (Christensen et al., 2000; Benjamins et al., 2001; Friml et al., 2004; Galvan-Ampudia and Offringa, 2007; Michniewicz et al., 2007; Robert and Offringa, 2008; Sukumar et al., 2009). In a phenotypic class quite distinct from the *nph3* and *mab4/enp/npy1* mutants, the *seth6* mutants (containing lesions in *NRL18*) exhibit a block in pollen germination and tube growth (Lalanne et al., 2004), suggesting that NRL functions are quite diverse indeed.

Members of the NRL protein family, in addition to displaying modular sequence conservation, exhibit modular structural features that are positionally conserved while sequence diverged (Figure 4A). Two of these structurally-conserved regions represent known protein-protein interaction motifs; a BTB (broad complex, tramtrack, bric à brac)/POZ (pox virus and zinc finger) domain (Albagli et al., 1995; Aravind and Koonin, 1999; Stogios et al., 2005) in the amino-terminal region, and a coiled-coil domain (Cohen and Parry, 1990; Lupas, 1996) in the carboxyl-terminal region (Motchoulski and Liscum, 1999; Sakai et al., 2000; Stogios et al., 2005). While no particular function can be inferred

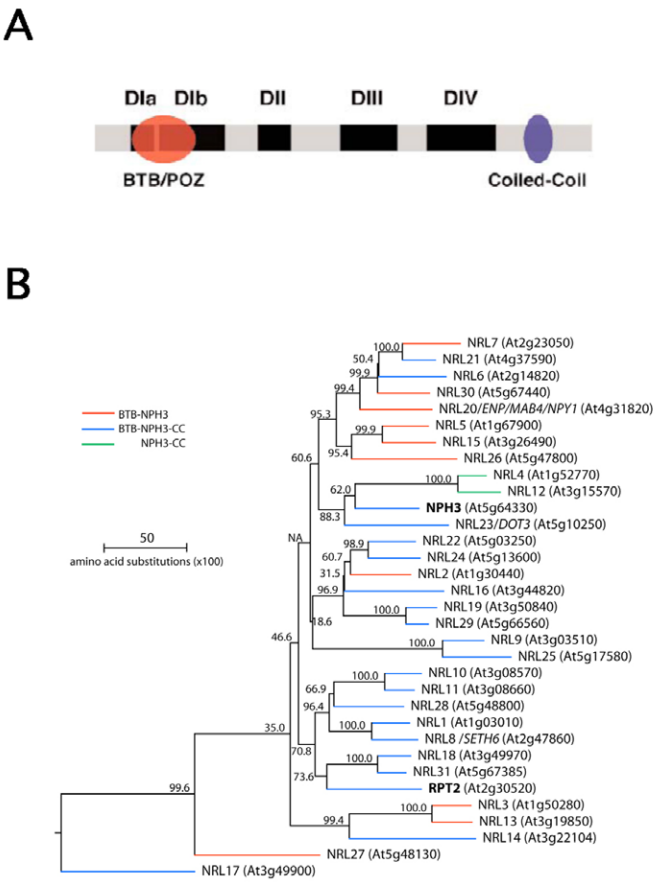

Figure 4. Consensus domain structure of the NPH3/RPT2 (NRL) protein family.

(A) The DIa, DIb, DII, DIII, and DIV regions (black bars) represent areas of sequence conservation among members of the NPH3/RPT2 protein family. The BTB/POZ (red region) and coiled-coil (blue region) domains represent structurally conserved motifs. While not all members of the family contain all of these domains (see cladogram in Figure 4B), each domain is present in both NPH3 and RPT2 (Motchoulski and Liscum, 1999; Sakai et al., 2000). Inter-domain regions (grey) while not sequence conserved exhibit moderate structural similarities from member to member (see http://www.biosci.missouri.edu/liscum/nph3-rpt2figs.html).

(B) Cladogram of the NRL protein family based on amino acid sequence obtained from Arabidopsis genome annotation (TAIR8) at TAIR. NRL protein sequences were aligned by ClustalW and the resulting ClustalW alignment was used to generate a rooted phylogenetic tree (Cladogram). Corresponding AGI numbers for a given NRL member is given in parenthesis.

from the presence of a BTB/POZ (hereafter referred to simply as BTB) or a coiled-coil domain, the fact that most of the NRL family members contain one or both (21 of 33 members, including NPH3 which contains both; Figure 4B) suggests that protein-protein interactions are an important feature of the biochemical function of this family.

While the subcellular localization of most members of the NRL family is currently unknown, NPH3, like phot1 (Briggs and Huala, 1999; Inada et al., 2004), has been shown to be associated with the plasma membrane (Motchoulski and Liscum, 1999; Lariguet et al., 2006; Pedmale and Liscum, 2007). In dark-grown wild-type seedlings NPH3 exists in a phosphorylated form (hereafter referred to as $NPH3^{DS}$; DS, dark state) that is rapidly converted into a dephosphorylated form in response to BL irradiation ($NPH3^{LS}$; LS, lit state) in a time dependent manner, but independent of fluence rate (Pedmale and Liscum, 2007; Tsuchida-Mayama et al., 2008). Moreover, $NPH3^{LS}$ is rapidly converted back into $NPH3^{DS}$ by merely placing the light-treated seedlings in darkness (Pedmale and Liscum, 2007; Tsuchida-Mayama et al., 2008). Since NPH3 and phot1 share the same sub-cellular space, it seemed possible that NPH3 might be a substrate for phot protein kinase activity. However, Pedmale and Liscum (Pedmale and Liscum, 2007) demonstrated that $NPH3^{DS}$ is formed in *phot1phot2* double mutants, indicating that neither phot1 nor phot2 is required for dark-dependent phosphorylation of NPH3. Interestingly, conversion of $NPH3^{DS}$ to $NPH3^{LS}$ in BL is phot1 dependent, while phot2 does not appear to play a role (Pedmale and Liscum, 2007; Tsuchida-Mayama et al., 2008). This suggests that the protein phosphatase dephosphorylating $NPH3^{DS}$ might function immediately downstream of phot1, and that phot1 might well be regulating the unknown phosphatase.

Pedmale and Liscum (Pedmale and Liscum, 2007) showed that dephosphorylation of NPH3 might be necessary for phototropism, since conversion of $NPH3^{DS}$ to $NPH3^{LS}$ was shown to be correlated with BL dependent phototropism. In a more recent study Tsuchida-Mayama and colleagues (Tsuchida-Mayama et al., 2008) came to the conclusion that conversion of $NPH3^{DS}$ to $NPH3^{LS}$ is not required for phototropic signaling. This latter conclusion was based largely on the observations that NPH3 phosphorylation incompetent mutants fail to rescue aphophototropism in a null-mutant background. However, closer examination of these results reveal that it may be premature to throw out the model proposed by Pedmale and Liscum (Pedmale and Liscum, 2007). For example, all of the potential phosphorylation sites examined by Tsuchida-Mayama and colleagues (Tsuchida-Mayama et al., 2008) were identified entirely through computational methods, and no report of *in vivo* confirmation currently exists. Even more importantly, the finding that mutation of a Ser/Thr to Ala results in apparently phototropically competent NPH3 protein (Tsuchida-Mayama et al., 2008) is entirely consistent with a model in which $NPH3^{LS}$ (dephosphorylated NPH3) is the active signaling state (Pedmale and Liscum, 2007) since those mutations would be expected to result in a constitutively active signaling state. The true test of the alternative model proposed by Tsuchida-Mayama and colleagues (Tsuchida-Mayama et al., 2008) would be to generate phosphorylation mimic mutants that lock NPH3 in a pseudo-phosphorylated state ($NPH3^{DS}$-like). Such mutations would prevent conversion of $NPH3^{DS}$ to $NPH3^{LS}$, thus directly testing the validity of the two opposing models.

Emergent Model: NPH3 as a Component of a CULLIN3-based Ubiquitin Ligase

Recent reports have demonstrated that BTB-domain containing proteins can participate as a substrate-specific adaptors in CULLIN3 (CUL3)-based E3 ubiquitin ligases, also known as CRL3s (CUL3-RING-ligase) (Geyer et al., 2003; Krek, 2003; Pintard et al., 2003; Xu et al., 2003; Willems et al., 2004; Dieterle et al., 2005; Figueroa et al., 2005; Gingerich et al., 2005; Petroski and Deshaies, 2005; Stogios et al., 2005; Weber et al., 2005). Interestingly, the activity of E3 ubiquitin ligases can be influenced by phosphorylation of its core components (Spanu et al., 1994; Glickman and Ciechanover, 2002; Schwechheimer and Calderon Villalobos, 2004), and the phosphorylation status of the substrates themselves can influence the ability of the E3 ligase to target those substrates (Spanu et al., 1994; Wang et al., 2004). Hence it seems plausible that NPH3, based on its sequence and structural properties (Motchoulski and Liscum, 1999; Inada et al., 2004; Celaya and Liscum, 2005; Pedmale and Liscum, 2007) represents a substrate adapter component of a CRL3, and that the conversion of $NPH3^{DS}$ and $NPH3^{LS}$ might constitute the 'on/off' switch for the activity of $CRL3^{NPH3}$ (Celaya and Liscum, 2005; Pedmale and Liscum, 2007). Given that BTB-containing proteins normally function as dimers/multimers (Stogios et al., 2005) and that NPH3 is a member of the larger NRL family, it seems appropriate to hypothesize that NPH3 can homodimerize with itself, or heterodimerize with other NRL family members, allowing a $CRL3^{NPH3/NRL}$ to target numerous substrates. Such an arrangement appears to be common with mammalian and fungal BTB-containing proteins. For example, homo- and heterodimerization of the mammalian BTB protein Keap1 allows for targeting of multiple target proteins for ubiquitination by $CRL3^{Keap1}$ (Lo and Hannink, 2006). Future studies on the biochemical function of NPH3 and identification of substrate(s) of $CRL3^{NPH3}$ will provide a wealth of new insights in how early phototropic signal transduction proceeds and the role that protein ubiquitination plays in these processes.

RPT2: A Modular Adapter for phot Signaling?

RPT2 (Table 1 and Figure 4B), the other founding member of the NRL family, was originally identified via a mutant allele that conditions reduced phototropism (Okada and Shimura, 1992). However, in the case of the *rpt2* mutant a phototropic defect is only obvious under high fluence rate BL ($\geq 10 \mu mol\ m^{-2}\ s^{-1}$) (Sakai et al., 2000; Inada et al., 2004). It thus appears that RPT2 functions over a fluence rate range similar to that in which phot2 functions (Sakai et al., 2000; Sakai et al., 2001) (Table 3). A parallel between *RPT2* and *PHOT2* is also observed at the level of transcript abundance, with both transcripts being detectable at only very low levels in etiolated seedlings but increasing in abundance in response to light with similar fluence rate and wavelength dependencies (Sakai et al., 2000; Sakai et al., 2001) (Table 3).

RPT2, like NPH3 (Motchoulski and Liscum, 1999; Lariguet et al., 2006), is a plasma membrane-localized protein that has been found to co-immunoprecipitate with phot1 in extracts from etiolated Arabidopsis seedlings (Inada et al., 2004). It also appears that RPT2 and NPH3 can heterodimerize through their amino-terminal BTB-domains (Inada et al., 2004), though this

may not be particularly surprising as BTB containing domains are known to mediate protein-protein interaction for homo- or heterodimerization (Ahmad et al., 1998a; Stogios et al., 2005). While Inada and colleagues proposed that RPT2 directly interacts with phot1 – largely based on weak interaction in yeast (Inada et al., 2004), the finding that RPT2 and NPH3 strongly interact in yeast suggests that RPT2 may co-immunoprecipitate in plant extracts with phot1 via interaction with NPH3, which interacts strongly and directly with phot1 *in vitro*, in yeast and *in planta* (Motchoulski and Liscum, 1999; Lariguet et al., 2006). The conditional phototropic phenotype of the *rpt2* mutant in comparison to the apparent complete aphototropic phenotype of the *nph3* mutants, along with the sequence and structural homologies between the RPT2 and NPH3 proteins (Motchoulski and Liscum, 1999; Sakai et al., 2000; Inada et al., 2004), suggest that RPT2 may have partial overlapping function with NPH3 in phototropic signaling but only under high fluence rate conditions. While it seems appropriate to speculate that RPT2 also participates in function of a CRL3 complex, either as a homodimer or as a heterodimer with NPH3, this has yet to be tested.

PKS1: A Bridge Between phot and phy Signaling?

PHYTOCHROME KINASE SUBSTRATE 1 (PKS1), while identified in a yeast-two-hybrid screen that utilized the carboxyl-terminus of phyA as a bait, is the first protein known to interact with both phyA and phyB in the cytosol (Fankhauser et al., 1999; Lariguet et al., 2003). Phys readily phosphorylate PKS1 both *in vitro* and *in vivo* in a light-dependent fashion, and it has been hypothesized that phosphorylated PKS1 negatively regulates phy function (Fankhauser et al., 1999; Schepens et al., 2008). *PKS1* is a member of a small gene family in *Arabidopsis* (*PKS1* to *PKS4*) with no predictable functional sequence motifs (Lariguet et al., 2003; Lariguet et al., 2006). Interestingly, BL stimulates the expression of *PKS1* (Lariquet, 2006), suggesting that PKS1 may also function in BL responses such as phototropism. In line with this possibility Lariquet and colleagues (Lariguet et al., 2006) have shown that *pks1pks2pks4* triple mutant seedlings exhibit reduced phototropism in low fluence rate BL, conditions under which phot1 operates as the primary phototropic photoreceptor (Celaya and Liscum, 2005; Holland et al., 2009). In the same study it was demonstrated that PKS1 is a plasma membrane-associated protein and that it physically interacts with both phot1 and NPH3 *in vitro* and *in planta* (Lariguet et al., 2006). It has recently been shown that PKS1 also positively regulates phot1-dependent BL-induced negative root phototropism in Arabidopsis by negatively regulating gravitropism (Boccalandro et al., 2008), and that it modulates phy-dependent positive root phototropism induced by RL (Molas and Kiss, 2008). A common theme emerging from such studies is that PKS proteins appear to regulate directional orientation of organs to various stimuli by influencing asymmetric growth (Lariguet and Fankhauser, 2004; Lariguet et al., 2006; Boccalandro et al., 2008; Schepens et al., 2008). How exactly the PKS proteins function biochemically is currently unknown, although it does appear that these proteins can function in both phy- and phot-dependent signaling pathways.

Other phot-Interacting Proteins: A 14-3-3 and a Dynein Light Chain-like Protein (VfPIP)

As discussed in the previous sections, three phot1-interacting proteins have been characterized that play roles in phototropic signaling. Two additional phot1-interacting proteins, a 14-3-3 and a dynein light chain-like protein (VfPIP, for phot1-interacting protein) have been identified in *Vicia faba* (Kinoshita et al., 2003; Emi et al., 2005), but their roles in phototropism have yet to be examined. The 14-3-3 protein was found through its reversible binding to Vfphot1a and Vfphot1b (paralogs of Arabidopsis phot1); binding that is dependent upon specific BL-induced autophosphorylation of the phot1 isoforms (Kinoshita et al., 2003; Inoue et al., 2008). Recently, it has been found that phot1 interacts with non-epsilon type 14-3-3 proteins in Arabidopsis as well, though no interactions have been observed as yet between phot2 and 14-3-3 proteins (Sullivan et al., 2009). Although it is presently not known how 14-3-3 proteins might influence phot1 signaling several possibilities exist: for example, 14-3-3 proteins are known to interact with a target protein to generate a scaffold so that other proteins can dock, to inhibit a target protein's activity, to change in subcellular localization of the target protein or to tag a protein for post-translational modification (Kinoshita et al., 2003; Ferl, 2004; Gampala et al., 2007). Emi and colleagues (Emi et al., 2005) proposed that VfPIP, identified by virtue of its ability to interact with Vfphot1a and found to localize to the cortical microtubules in guard cells, functions as a motor-proteins to mediate phot1-dependent stomatal opening in response to BL.

Ca^{2+} As a Second Messenger

It may not be too surprising given its pervasive role in intracellular signaling (Bush, 1993) to find that Ca^{2+} may play a role in the transduction of phototropic stimuli in higher plants (Gehring et al., 1990; Ma and Sun, 1997; Harada and Shimazaki, 2007). A study by Baum and colleagues (Baum et al., 1999) reported that a transient increase in cytoplasmic Ca^{2+} ($[Ca^{2+}]_{cyt}$) is observed in wild-type Arabidopsis seedlings exposed to BL, and that this response is severely impaired in the *phot1* mutant background. It was also shown that Ca^{2+} was moving into the cytosol across the plasma membrane, thus placing the necessary channel activity in the same intracellular compartment as phot1 - the plasma membrane. Use of a noninvasive ion-selective microelectrode ion flux measurement (MIFE) technique allowed Babourina and colleagues (Babourina et al., 2002) to measure the net Ca^{2+} ion flux across the plasma membrane and cell wall in Arabidopsis seedlings. It was found that in *phot1* and *phot1phot2* mutants BL did not initiate the immediate influx of Ca^{2+} in to the cytoplasm, while Ca^{2+} influx in *phot2* mutant seedlings was comparable to wild-type seedlings. These findings indicate that BL-induced influx of Ca^{2+} from the apoplastic space occurs primarily through the action of phot1 (Babourina et al., 2002).

BL dependent opening of plasma membrane calcium channels characteristic of Ca^{2+} influx is reported to be dependent on phot1 in mesophyll cells of Arabidopsis leaves but independent of photosynthetic activity (Stoelzle et al., 2003). In addition to phot1, phot2 is also capable in eliciting rapid Ca^{2+} influx at higher fluence rates (Harada et al., 2003). The investigators used the biolumi-

nescent Ca^{2+} indicator aequorin in Arabidopsis *phot1*, *phot2* and *phot1phot2* mutant plants to demonstrate that phot1 and phot2 contributed additively in elevation of free $[Ca^{2+}]_{cyt}$. Given the differences in photosensitivities of phot1 and phot2, it is not surprising that phot2 efficiently mediates the influx of Ca^{2+} at fluence rates of BL between 1 and 250 μmol m^{-2} s^{-1}, whereas phot1 is effective in the 0.1 to 50 μmol m^{-2} s^{-1} range. At this point it is unclear if phot2 is able to mediate Ca^{2+} influx from the apoplast independent of phot1 since the two studies had conflicting results (Babourina et al., 2002; Harada et al., 2003). Moreover, given the overlapping but distinct roles of phot1 and phot2 in mediating BL responses, it is possible that an individual phot might trigger the release of free $[Ca^{2+}]_{cyt}$ from different stores for specific responses. It is interesting to note that the rapid transient BL-induced increase in $[Ca^{2+}]_{cyt}$ is observed in both *cry1* and *cry2* mutants (Baum et al., 1999; Stoelzle et al., 2003), suggesting that phots are the only class of BL receptors responsible for this plasma membrane-localized response.

BL is also known to induce the rapid phosphorylation and activation of plasma membrane H^+-ATPase in a phot1- and phot2-dependent manner (Kinoshita and Shimazaki, 1999; Kinoshita et al., 2001). Harada and Shimazaki (Harada and Shimazaki, 2009) have shown that H^+-ATPase activation is prerequisite to the phot-dependent BL-induced $[Ca^{2+}]_{cyt}$ increase. Another possible regulatory mechanism has also been reported by Chen and colleagues (Chen et al., 2008) who found that BL, acting through phots, suppresses steady-state transcript levels of *INOSITOL POLYPHOSPHATE 5-PHOSPHATASE 13* (*5PTase13*), a gene encoding an enzyme that dephosphorylates inositol polyphosphates ($Ins_{(1,4,5)}P3$, $Ins_{(1,3,4,5)}P4$ or $PtdIns_{(4,5)}P2$). The authors proposed that in darkness 5PTase13 enzyme activity is high due to a higher level of protein and that the reduced levels of inositol polyphosphates keep plasma membrane Ca^{2+} channel activity low, thus keeping the $[Ca^{2+}]_{cyt}$ low. In contrast, in BL 5PTase13 enzyme levels are suppressed thereby leading to increased levels of inositol polyphosphates, Ca^{2+} channel activity, and an increase in free $[Ca^{2+}]_{cyt}$. At present it is not known how well, if at all, the temporal and photobiological properties of 5PTase13 enzyme and Ca^{2+} levels correlate.

While the role of BL-induced changes in $[Ca^{2+}]_{cyt}$ in phototropic signaling remains to be determined it is worth noting that Ca^{2+} has also been proposed as a possible second messenger for gravitropic signaling (Trewavas and Knight, 1994; Sinclair and Trewavas, 1997; Chen et al., 1999). Moreover, identification of calmodulin-like TOUCH3 (TCH3) protein and the calcium binding motif containing PINOID-BINDING PROTEIN 1 (PBP1) as PID-interacting proteins provides evidence for the existence of cross-talk between calcium and auxin movement (Benjamins et al., 2003). Though PID action in phototropic signaling has yet to be described, PID has been shown to be required for the lateral relocalization of PIN1 (Friml et al., 2004) and to function in gravitropism (Benjamins et al., 2001). Interestingly, PIN1 has also been shown to be relocalized in response to phototropic stimulation in a phot1-dependent manner (Blakeslee et al., 2004). As will be discussed in the following section auxin relocalization represents a common link between various tropic responses (Firn and Digby, 1980; Poff et al., 1994; Kaufman et al., 1995; Estelle, 1996). It is therefore attractive to speculate that the regulation of PIN1 localization and auxin movement by both PID and phot1, members of the same subclade of protein kinases, the AGCVIII kinases (Galvan-Ampudia and Offringa, 2007; Robert and Offringa, 2008), may utilize Ca^{2+} and Ca^{2+}-binding proteins as common signaling elements.

Differential Auxin Localization and Changes in Gene Expression

Regulation of auxin transport and accumulation

Auxins have long been implicated as regulators of tropic growth responses (Iino, 1990; Kaufman et al., 1995). In fact, auxin is a linchpin in most mechanistic models of phototropism (and gravitropism) (Estelle, 1996; Chen et al., 1999; Liscum and Stowe-Evans, 2000; Hoshino et al., 2007). The Cholodny-Went theory (Went and Thimann, 1937) provides much of the basis for the proposed central role of auxin in tropic responses. In brief, this theory holds that tropic stimuli induce differential lateral auxin transport that leads to the unequal distribution of auxin, and hence growth, in the two sides of a curving organ. While differential auxin transport, or accumulation, has been difficult to demonstrate in many cases (Trewavas et al., 1992), it has become clear through the use of Arabidopsis mutants that transport of, and response to, auxin is prerequisite for the development of tropic curvatures (Bennett et al., 1996; Estelle, 1996; Watahiki and Yamamoto, 1997; Chen et al., 1998; Luschnig et al., 1998; Muller et al., 1998; Rouse et al., 1998; Stowe-Evans et al., 1998; Utsuno et al., 1998; Chen et al., 1999; Marchant et al., 1999; Palme and Galweiler, 1999; Rosen et al., 1999; Yamamoto and Yamamoto, 1999; Harper et al., 2000; Rashotte et al., 2000; Geldner et al., 2001; Swarup et al., 2001; Friml et al., 2002; Tanaka et al., 2006). Numerous studies have shown that auxin efflux processes, which are necessary for the establishment of a lateral gradient of auxin (Lomax et al., 1995; Friml et al., 2002), may be regulated via reversible protein phosphorylation (Bernasconi, 1996; Garbers et al., 1996; Delbarre et al., 1998; Christensen et al., 2000; Rashotte et al., 2001; Michniewicz et al., 2007). These findings provide a compelling potential connection between the phots, which are light-activated protein kinases (Christie et al., 1998; Sakai et al., 2001), and the differential auxin gradients that have been observed in seedlings irradiated with unilateral BL (Iino, 1990; Esmon et al., 2006).

Several possible biochemical pathways from phot activation to changes in auxin transport can be postulated. First, a direct phot1/phot2-dependent phosphorelay involving currently unidentified protein kinases, or via PID, might lead to an altered auxin transport activity. Alternatively, phots might activate/modulate auxin transport through an indirect pathway that utilizes Ca^{2+} as a second messenger. In this latter scenario phot1 (phot2)-dependent increases in cytoplasmic Ca^{2+} levels might lead to activation of a Ca^{2+}-dependent protein kinase (CDPK) (Satterlee and Sussman, 1998; Harmon et al., 2000) or PID kinase via the action of Ca^{2+}-binding PBP1 or TCH3, which would in turn phosphorylate an auxin transport complex and thus alter its activity. A third possible outcome of phototropin activation is the modulation of auxin transporter localization, rather than the activity of single molecules. For example, relocalization of auxin efflux carriers from a basal to lateral region of a cell would result in a shift from basipetal to lateral auxin transport. Geldner and colleagues (Geld-

ner et al., 2001) have shown that the apparent static asymmetric localization of PIN1, one member of a family of auxin efflux carriers (Chen et al., 1998; Luschnig et al., 1998; Muller et al., 1998; Utsuno et al., 1998; Palme and Galweiler, 1999; Titapiwatanakun et al., 2009), actually results from a rapid actin-dependent cycling of PIN1 between the plasma membrane and endosomal compartments. Interestingly, though the mechanism has yet to be resolved, phot1 has been shown to be genetically required for the redistribution of PIN1 in the shaded flank of a phototropically-stimulated seedling (Blakeslee et al., 2004). It is also worth noting that it has been found that PID can directly phosphorylate the PIN1 auxin efflux carrier to alter its endocytotic cycling (Skirpan et al., 2009; Huang et al., 2010; Zhang et al., 2010), suggesting that phot1 protein kinase activity could be linked to this process. Another auxin efflux carrier, PIN3, has been shown to localize to all faces of the plasma membrane in non-tropically stimulated cells, but relocalize to the lateral faces following gravitropic stimulation (Friml et al., 2002). Though no phototropic stimulation-dependent relocalization of PIN3 has been demonstrated (Blakeslee et al., 2004), *pin3* mutations render seedlings defective in both gravitropic and phototropic responses (Friml et al., 2002), indicating that PIN3 function is important for phototropism.

As second class of auxin transporters, the ABCB subgroup of ABC transporter superfamily (Verrier et al., 2008), has also been associated with tropic responsiveness. For example, mutations in *ABCB19* (also known as *PGP19*) result in enhanced phototropic and gravitropic responses in Arabidopsis seedlings (Noh et al., 2003; Blakeslee et al., 2004). In addition, PIN1 is mislocalized in *abcb19* mutants in manner similar to that observed when wild-type seedlings are exposed to BL (Noh et al., 2003; Blakeslee et al., 2004). Interestingly, steady-state levels of *ABCB19* mRNA are suppressed through the action of phys and crys (Nagashima et al., 2008), suggesting yet another mechanism by which these other photoreceptors might influence phot-dependent phototropism.

Given the overlapping localization of phot, PIN and ABCB proteins in the plasma membrane of elongating cells is seems plausible that phots may influence auxin transport by directly interacting with and modulating the activity/localization of the latter proteins. Alternatively, phot activation could also lead indirectly to changes in the activity/localization of auxin transporters, possibly through phosphorylation or Ca^{2+}-dependent changes in the activity of a variety of regulator proteins, such as the NPA (naphthylphthalamic acid)-binding protein (Muday et al., 1993), 3-phosphoinositide dependent kinase 1 (PDK1) (Zegzouti et al., 2006) and the calossin-like protein BIG (Gil et al., 2001). Determining exactly how phot activation leads to changes in auxin transporter activity/localization will be one of the most active areas of phototropic research over the next few years.

Changes in auxin-dependent transcription

In recent years significant advances have been made in understanding how differential auxin gradients established in response to tropic stimulation are interpreted at a molecular level to give rise to differential growth patterns. Critical to these advances was the identification and characterization of semi-dominant mutations in the *NON-PHOTOTROPIC HYPOCOTYL 4/MASSUGU 1/TRANSPORT INHIBITOR RESISTANT 5 (NPH4/MSG1/TIR5)* locus (hereafter referred to as *NPH4*) (Table 1) of Arabidopsis that disrupt multiple differential growth responses in aerial tissues, including phototropism and gravitropism, without altering overall growth and development of the plant (Liscum and Briggs, 1995, 1996; Ruegger et al., 1997; Watahiki and Yamamoto, 1997; Stowe-Evans et al., 1998; Watahiki et al., 1999). These phenotypes, together with the findings that the *nph4* mutants exhibit severely impaired auxin-induced stem bending (Watahiki and Yamamoto, 1997), stem growth inhibition (Watahiki and Yamamoto, 1997; Stowe-Evans et al., 1998), and gene expression responses (Stowe-Evans et al., 1998), suggested that the NPH4 protein functions as a modulator of auxin-dependent differential growth. Map-based cloning of the *NPH4* gene revealed that it encodes the auxin response factor ARF7 (Harper et al., 2000), a member of a large family of transcription factors whose activities are regulated by auxin (Guilfoyle et al., 1998; Liscum and Reed, 2002). NPH4/ARF7 functions as a transcriptional activator in transient expression assays (Ulmasov et al., 1999), consistent with the impaired auxin-induced gene expression profiles observed in the *nph4/arf7* mutants (Stowe-Evans et al., 1998). It therefore appears that localized changes in gene expression are at least one of the likely consequences of a differential auxin gradient established in response to phototropic stimulation (Harper et al., 2000; Stowe-Evans et al., 2001).

NPH4/ARF7 has been shown to interact with numerous members of the Aux/IAA family of auxin-induced proteins that function as dominant repressors of ARF activity (Tiwari et al., 2001; Tiwari et al., 2004; Li et al., 2009). Of particular interest in the context of tropic growth regulation are the MASSUGU2 (MSG2/IAA19) and AUXIN RESISTANT5 (AXR5/IAA1) proteins, in which dominant gain-of-function mutations condition severely impaired phototropic and gravitropic responses (Park et al., 2002; Tatematsu et al., 2004; Yang et al., 2004). These findings, together with a developing and sophisticated understanding of how auxin regulates changes in gene expression, have allowed the development of a relatively simple model for tropic growth can occur in response to auxin-responsive transcription (Tatematsu et al., 2004; Holland et al., 2009). In brief, elevated levels of free auxin, like those induced differentially across a phototropically-induced stem (Esmon et al., 2006; Haga and Iino, 2006), promote the 26S proteasome-dependent degradation of Aux/IAA proteins, such as MSG2/IAA19 and AXR5/IAA1, through a targeting mechanism mediated by the $CRL1^{TIR1}$ (also known as SCF^{TIR1}) complex that contains the auxin receptor TIR1 (Tan et al., 2007). Given that MSG2/IAA19 and AXR5/IAA1 would be found as heterodimers with NPH4/ARF7 under low auxin conditions thus repressing activity of the latter, their auxin-induced degradation would therefore allow homodimerization of NPH4/ARF7 and subsequent transcriptional upregulation of 'auxin-responsive genes' (Tatematsu et al., 2004; Celaya and Liscum, 2005; Holland et al., 2009). In an interesting twist to this model, it is likely that *MSG2/IAA19* and *AXR5/IAA1* themselves represent target genes for NPH4/ARF7 regulation (Stowe-Evans et al., 1998; Tatematsu et al., 2004), with the transcription and translation of these genes providing a feed-back mechanism to rapidly dampen the auxin response (Liscum and Reed, 2002).

A microarray approach was utilized to identify potential transcriptional targets of NPH4/ARF7 under tropically-responsive conditions. Several, tropic stimulus-responsive (TSI) transcripts were identified by comparing expression profiles between op-

posing flanks of phototropically- and gravitropically-stimulated hypocotyls of *Brassica oleracea* (Esmon et al., 2006). Among the TSI transcripts identified were *EXPANSIN (EXP) 1* and *8*, whose steady-state mRNA levels were shown to be up-regulated in a tropic stimulation and auxin-dependent fashion in the flank farthest from the tropic stimulation- prior to the development of a differential growth response (Esmon et al., 2006). These genes are particularly interesting because they encode proteins that are thought to break H-bonds between cellulose microfibrils and hemicellulose in the cell wall to increase wall extensibility, allowing for increased turgor-driven cell elongation (Cosgrove, 2005; Yennawar et al., 2006; Durachko and Cosgrove, 2009). Two *GH3* genes (*GH3.5* and *GH3.6/DFL1*), known to encode enzymes that catalyze the conjugation of free IAA to amino acids (Staswick et al., 2005), were also identified in this study. While the steady-state levels of these genes increased in the same spatial region and with similar tropic stimulation- and auxin-dependencies as the *EXP* genes, the timing of expression was considerably delayed in comparison to the latter genes, consistent with the notion that the proteins encoded by the *GH3* genes would act to suppress auxin responsiveness by decreasing the free auxin pool (Esmon et al., 2006). Not surprisingly, given the auxin-dependencies of the TSI genes, the promotor regions of each of these genes contain at least one auxin responsive element (AuxRE) (Esmon et al., 2006) known to provide a binding site for ARF proteins, like NPH4/ARF7 (Hagen and Guilfoyle, 2002; Liscum and Reed, 2002). Consistent with this finding it was also found that auxin-induced expression of the TSI genes in Arabidopsis is dependent upon the presence of NPH4/ARF7 (Esmon et al., 2006). With the functional genomics tools now at our disposal, additional targets for NPH4/ARF7 regulation should not remain elusive for long.

RESPONSE MODULATION VIA SECONDARY PHOTOSENSORY EVENTS

Plants utilize a process known as photosensory adaptation to modify their sensitivity and responsiveness to changes in their light environment that occur throughout diurnal and seasonal cycles (Galland, 1989, 1991). Photosensory adaptation can be separated into two types of phenomena: 1) sensor adaptation, and 2) effector adaptation. Sensor adaptation was introduced earlier in the context of a potential role for phot1 and phot2 light-induced phosphorylation and the phototropic desensitization process. In this section we will discuss what is known about the molecular properties of effector adaptation processes as they relate to phototropism in Arabidopsis. In particular we will focus on the amplification of signal outputs from the phot1-dependent transduction pathway that lead to enhancement of a basal phototropic response in etiolated seedlings.

By definition photosensory adaptation responses include rapid desensitization components (discussed earlier), as well as slower recovery and responsiveness modulation (enhancement) components (Galland, 1989, 1991). Recovery of phototropic sensitivity occurs within a few minutes of onset of irradiation, while enhancement takes place over a period of hours (Zimmerman and Briggs, 1963; Iino, 1990; Poff et al., 1994). For example, preirradiation results in a decrease in the lag times for recovery of phototropic sensitivity (Zimmerman and Briggs, 1963; Janoudi et al., 1992; Liu and Lino, 1996) and enhancement of curvature (Chon and Briggs, 1966; Janoudi and Poff, 1991; Liu and Iino, 1996). Recovery of phototropic sensitivity and response enhancement appear to be mechanistically related and reflect effector rather than sensor adaptation processes (Iino, 1990; Poff et al., 1994).

phyA Is the Major Effector of phot1-Dependent Phototropism

Although BL can induce phototropic enhancement in monocot (Blaauw and Blaauw-Jansen, 1970; Iino, 1988) and dicot (Janoudi and Poff, 1991) seedlings, RL can also induce phototropic enhancement (Figure 5) implicating a RL-absorbing receptor in the enhancement response (Iino, 1990; Poff et al., 1994). Action spectroscopy and partial RL/FR reversibility (Janoudi and Poff, 1992; Liu and Iino, 1996), together with the absorptive properties of phys (Butler, 1964; Pratt and Briggs, 1966; Vierstra, 1983), have suggested that one or more phy can mediate phototropic enhancement under both BL alone and BL plus RL conditions (Liscum and Stowe-Evans, 2000; Whippo and Hangarter, 2004). Analyses of phy-deficient mutants of Arabidopsis provide compelling support for this hypothesis and indicate that both phyA and phyB (Table 1) function as regulators of phototropic enhancement. In particular, phyA appears to act as the major receptor in low fluence conditions, while phyB dominates under high fluences (Parks et al., 1996; Janoudi et al., 1997a; Janoudi et al., 1997b). As already discussed, Han and colleagues have found that phyA activation by RL can inhibit BL-induced internalization of phot1 (Han et al., 2008). This finding, together with the aforementioned photobiological properties, suggest that phyA-dependent enhancement of phototropism could result from more phot1 being retained at the plasma membrane to allow more signal transduction, without actually altering phot1 sensitivity.

Phys have also been implicated as upstream modulators of both auxin transport (Eliezer and Morris, 1980; Behringer and Davies, 1992; Jensen et al., 1998; Shinkle et al., 1998) and auxin-regulated gene expression (Oyama et al., 1997; Soh et al., 1999; Steindler et al., 1999; Tian and Reed, 1999; Nagpal et al., 2000). While one can certainly imagine how phys could influence auxin transport or response via alteration in phot1 localization, it is worth noting that the transcription of a large subset of genes, in the range of ~10% of the genome, appears to be regulated by phyA (Tepperman et al., 2001). Direct phyA-dependent transcriptional regulation could provide an additional means to modulate auxin levels in the plant, quite independent from phot function, which does not appear to directly regulate transcription (Ohgishi et al., 2004). By the ability to tightly control the expression of a suite of genes, phyA is able to rapidly deploy genes leading to a cascade in signaling. Given the apparent role of lateral auxin gradients in the establishment and maintenance of phototropic responses (Went and Thimann, 1937; Iino, 1990; Kaufman et al., 1995), and the transcriptional responses likely to result from such gradients (Stowe-Evans et al., 1998; Harper et al., 2000; Esmon et al., 2006), a phy-dependent increase in auxin responsiveness represents an ideal mechanism by which phototropic enhancement could occur (Liscum and Stowe-Evans, 2000).

Compelling support for this contention has been obtained through studies of the *nph4/arf7* mutants. In particular, while *nph4/arf7* null mutants are aphototropic in low fluence rate BL (Liscum and Briggs, 1995, 1996), they retain a strong phototropic

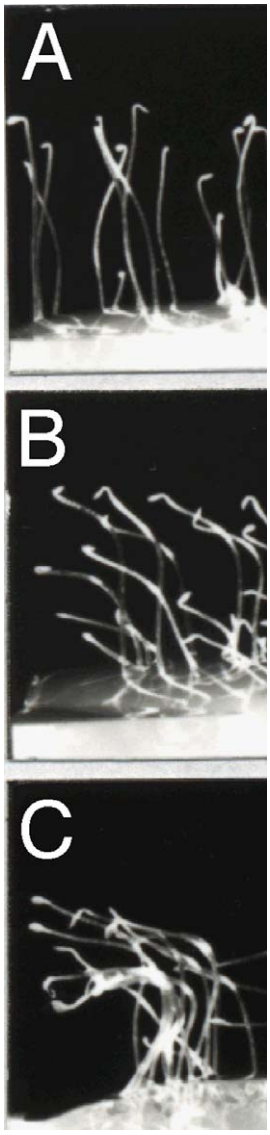

Figure 5. Phytochrome-induced enhancement of phot1-dependent phototropism in Arabidopsis.

(A) Three-d-old etiolated seedlings mock-irradiated for 8 h.
(B) Three-d-old etiolated seedlings mock-irradiated for 4 h, then exposed to 4 h of unilateral blue light (λ_{max} = 436 nm, 30 nm half-band; at a fluence rate of 0.1 µmol m^{-2} s^{-1}) from the left.
(C) Three-d-old etiolated seedlings exposed to 4 h of red light (λ_{max} = 660 nm, 30 nm half-band; at a fluence rate of 0.3 µmol m^{-2} s^{-1}) from above, then 4 h of unilateral blue light (λ_{max} = 436 nm, 30 nm half-band; at a fluence rate of 0.1 µmol m^{-2} s^{-1}) from the left.

response in high fluence rate BL (T. Campbell, E.L. Stowe-Evans, and E. Liscum, unpublished), or other irradiation conditions (e.g., low fluence rate BL plus RL) that stimulate both phot1 activity and significant phy Pr to Pfr photoconversion (Liscum and Briggs, 1996; Stowe-Evans et al., 2001). Not only does the action of phyA predominate in the phototropic enhancement response of etiolated wild-type seedlings (Parks et al., 1996; Janoudi et al., 1997a; Janoudi et al., 1997b; Stowe-Evans et al., 2001), but it also appears to be the major modulatory photoreceptor for recovery of response in the *nph4/arf7* background (Stowe-Evans et al., 2001). Together these results indicate that phyA action is able to suppress the deficiency in auxin-dependent gene expression conditioned by the loss of NPH4/ARF7. The simplest hypothesis to explain this phyA-dependent phototropic response in the complete absence of NPH4/ARF7 activity is that another ARF may respond to phyA signaling by activating the expression of genes that NPH4/ARF7 would otherwise activate (Figure 6). Given that NPH4/ARF7 activity appears genetically limiting (Liscum and Briggs, 1996; Stowe-Evans et al., 1998), this hypothesis is also consistent with the phyA-dependent phototropic enhancement response in wild-type where the second ARF would stimulate additional gene expression beyond that stimulated by the activity of NPH4/ARF7.

Models for phyA-Dependent Changes in ARF Activity

Two mechanistic explanations for the aforementioned hypothesis seem most probable. First, phyA action might lead to increased auxin content within the hypocotyl as a result of alterations in auxin transport (basipetal, lateral, or some combination thereof) or metabolism. Hence, any differential auxin accumulation in a phototropically-stimulated hypocotyl induced via a phot1-dependent response pathway would be enhanced, potentially resulting in partial activation of an ARF with a lower sensitivity to auxin (Figure 6a). Alternatively, phyA signaling might condition increased auxin sensitivity of a redundant ARF system via changes in expression or activity of that ARF protein (Figure 6b).

Relative to the first model it is worth noting that Stone and colleagues (Stone et al., 2008) employed a second-site enhancer screen to identify mutations in a *nph4/arf7*-null mutant background that would lead to complete loss of phototropic responsiveness in RL plus BL conditions where phyA activity normally suppresses the aphototropic phenotype observed in BL alone. Of the three enhancer mutations identified the *modifer of arf7 phenotypes 1* (*map1*) mutation was shown to be allelic to *AUX1* (Stone et al., 2008), a member of a small family of high-affinity auxin influx carriers (Swarup et al., 2004; Yang et al., 2006; Kerr and Bennett, 2007). The *map1/aux1-201* mutation was shown to be a missense allele converting Ala_{94} to Val within the second transmembrane span of AUX1 (Stone et al., 2008). While *map1/aux1-201* was identified as an enhancer of *nph4/arf7* phototropic defects, this *aux1* allele, as well as several previously identified missense alleles were shown to also condition subtle but significant reductions in phot1-dependent BL-induced phototropism even in the presence of normal NPH4/ARF7 activity (Stone et al., 2008). These and other results led to the proposal that phyA influences AUX1 activity (and possibly *AUX1* mRNA expression) to increase local symplastic auxin concentrations within the elongation zone of the hypocotyl/stem such that activation of another ARF(s) with lower auxin sensitivity leads to enhanced phototropic responsiveness in the presence of NPH4/ARF7 activity and to partial recovery of responsiveness in the absence of NPH4/ARF7 (Stone et al., 2008).

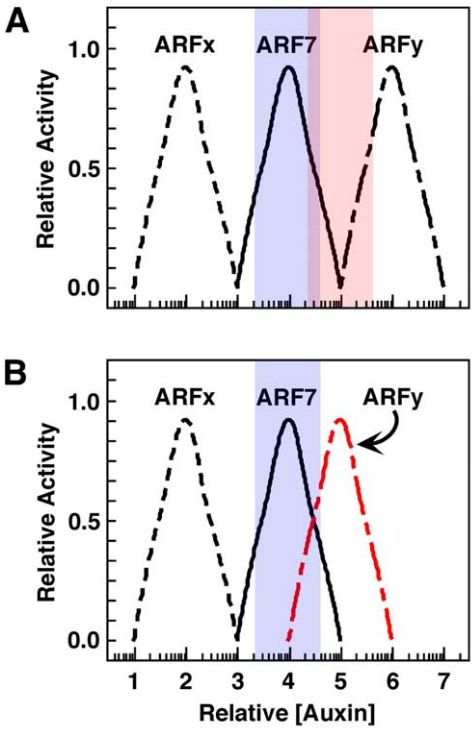

Figure 6. Working models to explain the phytochrome A-induced enhancement of phototropin-dependent phototropism in wild-type Arabidopsis seedlings and the recover of response in nph4 mutants lacking the auxin response factor ARF7.

From studies of the nph4/arf7 mutants it appears that phyA-dependent increases in the phototropic response of etiolated hypocotyls occur because of a partial activation of a second ARF (Stowe-Evans et al., 2001). Two obvious models can be developed. Both models assume that when multiple ARFs are expressed in the same cell any one ARF can specifically regulate the expression of auxin-responsive genes involved in a distinct biological phenomenon because of differences in the auxin sensitivities of the different ARFs (Liscum and Reed, 2001). First (A) phyA activation could lead to changes in auxin transport and/or metabolism leading to increases in auxin concentration on the side away from light (red block), above that induced by phot1 activation alone (blue block). Whereas the auxin concentration induced by phot1 action alone would result only in the activation of NPH4/ARF7, the auxin concentration established under both phot1 and phyA activating conditions would lead to the activation of both NPH4/ARF7 and ARFy. Alternatively (B) phyA action could lead to changes in the auxin sensitivity of ARFy. Note shift of ARFy response curve (red line) to lower auxin concentration range as compared to panel A. These models are not mutually exclusive, but each can account for the increase in phototropic response of wild-type seedlings, as well as the partial recovery of response in the nph4/arf7 null mutants.

While to date there is no direct experimental evidence in support of the model in which phyA activity increases auxin sensitivity through changes in ARF activity or expression, recent findings with respect to another conditional phototropic phenotype of *nph4/arf7*-null mutants suggest this model has merit. It had previously been shown that exposure to ethylene prior to, or concomitant with, exposure to directional BL could, like phyA activation (Stowe-Evans et al., 2001), partially suppress the aphototropic phenotype of *nph4/arf7*-null mutants observed in BL alone (Harper et al., 2000). Stone and colleagues (Stone et al., 2008) were able to demonstrate that the combination of a *nph4/arf7* mutation with loss-of-function mutations in *ARF19*, the most closely related ARF to NPH4/ARF7 (Remington et al., 2004), renders Arabidopsis seedlings incapable of exhibiting BL-induced phot1-dependent phototropism with or without ethylene exposure. Interestingly, *nph4/arf7arf19* double mutants still recover BL-induced phototropism when phyA is activated (Stone et al., 2008). These findings demonstrate that ARF19 is sufficient for the ethylene-dependent suppression of *nph4/arf7* aphototropism but not the phyA-dependent response. What makes this finding particularly interesting within the context of the model introduced above is the finding that *ARF19* mRNA expression is up-regulated in response to ethylene exposure (Li et al., 2006), thus providing an obvious explanation for the ARF19-dependent phenotype (Stone et al., 2008). While genetic support for a similar model of increased ARF activity does not currently exist for the phyA-dependent response, it is intriguing that the *map3* mutation (currently uncloned) influences the phyA-response specifically in much the same way the *arf19* mutations are specific to the ethylene response (Stone et al., 2008).

Redundant ARF function could also be influenced by phyA through promotion of Aux/IAA degradation. It is now well established that Aux/IAA proteins are targeted for 26S proteasome-dependent degradation by the CRL1/SCF^{TIR1} E3 ubiquitin-ligase complex (Gray and Estelle, 2000; Ramos et al., 2001; Schwechheimer et al., 2001; Dharmasiri et al., 2005; Kepinski and Leyser, 2005; Quint and Gray, 2006; Dos Santos Maraschin et al., 2009). In yeast and flies, many proteins targeted by a CRL1/SCF complex are first phosphorylated (Patton et al., 1998; Maniatis, 1999; Koepp et al., 2001). Interestingly it has been shown that phyA can interact with and phosphorylate Aux/IAA proteins *in vitro* (Colon-Carmona et al., 2000). Thus it seems plausible that phyA could influence the auxin sensitivity of a redundant ARF(s) by promoting, through phosphorylation, ubiquitylation and subsequent degradation of an Aux/IAA protein(s) that normally inhibits the activity of the redundant ARF(s). Although this possibility remains untested at present, protein turnover does appear to be at least one of the components of phyA-dependent recovery of phototropism in *nph4/arf7* mutants since *nph4/arf7axr1* double mutant seedlings fail to exhibit any phototropic response (E. L. Stowe-Evans, R. M. Harper, and E. Liscum, unpublished). *AXR1* (Table 1) encodes one of the two components (the other being ECR1) of a heterodimeric ubiquitin-E1-like enzyme that functions upstream of the CRL1/SCF^{TIR1} complex (del Pozo and Estelle, 1999; Gray and Estelle, 2000). Not surprisingly, *axr1* single mutants also exhibit impaired phototropic responses (Watahiki et al., 1999; Yang et al., 2004).

ECOLOGICAL AND EVOLUTIONARY SIGNIFICANCE OF PHOTOTROPISM

In contrast to the controlled and relatively simply environmental conditions plants find themselves in under laboratory or growth chamber conditions, growth in natural habitats results in exposure to large variations in all sorts of environmental stimuli on temporal and spatial scales. One of the challenges that plants have to

adapt to is the fluctuation in light quality and quantity through the course of the day, as well as by surrounding vegetation. Given the ubiquitous nature of phototropism within the plant kingdom, and its potential to dramatically increase the photosynthetic foraging capacity of a plant, it seems obvious to expect that the genes controlling this response have been under positive selective pressure during the evolution of different land plants. Yet, despite the potential ecological and evolutionary significance of phototropism, until recently no one had even asked: If two plants are growing in a shaded or light-limited environment, would the one exhibiting a stronger phototropic response have an adaptive advantage over the one with a weaker response? Why hadn't such a study been done until recently; could it be that such a test sounds easy but in fact has been quite difficult to design and execute? Just by the way the aforementioned question is posed - "if…the one exhibiting a stronger phototropic response has an adaptive advantage over the one with a weaker response?" - it is clear that this question has been extremely difficult to ask since it requires that one has access to two plants, presumably within the same species, with dramatically different phototropic potentials. With the identification of mutants in Arabidopsis that exhibit altered phototropic response the aforementioned question could finally be addressed.

Galen and colleagues (Galen et al., 2004) examined the fitness of *phot1*, *phot2* and *nph3* mutants in comparison to wild-type plants and found that each of these loci imparts a significant fitness advantage to young Arabidopsis seedlings that are germinated under simulated and natural canopy litter conditions. In particular, it was observed that *phot1, phot2* and *nph3* mutants had reduced lifetime fitness compared to wild-type, with phot1 and NPH3 contributing most prominently to fitness during seedling germination and emergence, and phot2 contributing post emergence of the seedling from the soil (Galen et al., 2004). Given the known fluence rate sensitiveness of phot1 and phot2 these observations were not, in hindsight, that surprising. Consistent with these findings under natural environmental conditions, Takemiya and colleagues (Takemiya et al., 2005) found that phot1 and phot2 promote at least three-fold higher biomass production in growth chamber-grown plants given RL sufficient to saturate the photosynthetic response but supplemented with low fluence rate BL conditions, as compared to plants grown in RL alone. Both of these studies indicate that phots provide adaptive value with respect to establishment and growth of plants, yet they do not address how phot activity impacts physiology to derive this adaptive value.

Negative phototropism and positive gravitropism direct directional growth of plant roots deeper in the soil for water and nutrients. A plants water status reflects the balance between absorption of water through the roots and transpiration through the stomatal pores in the leaves. Interestingly, both negative root phototropism (leading to increased access to soil-borne water) and stomatal opening (leading to water loss) are mediated by phots. How these two BL-induced spatially separated processes are coordinated is largely a mystery. However, it appears that phot1 function confers an adaptive advantage to plants growing under water-limited conditions (Galen et al., 2004). While the role of phot1-mediated stomatal opening was not specifically addressed, the investigators showed that roots of *phot1*-null mutants exhibited largely random growth patterns compared to wild-type or *PHOT1* transgene-complemented *phot1* mutant plants, leading to very shallow root growth relative to soil depth. Thus in dry soil conditions roots of *phot1* mutant plants simply do not penetrate the soil deep enough to access the limited water (Galen et al., 2007b; Galen et al., 2007a). Interestingly the aberrant root phenotypes of the *phot1* mutant are accentuated in dry *versus* wet conditions suggesting that there is interplay between drought and phot1 sensing-response systems (Galen et al., 2007b; Galen et al., 2007a).

The potential fitness advantages of maintaining phototropic responsiveness may be further increased by the co-opting of multiple photoreceptor systems in the modulation of phototropic response. For example, if phototropism was an all-or-nothing response, controlled solely by the differential activation of phot1 or phot2 a seedling could be "misled" into bending towards an unsuitable source of light. It makes intuitive sense that the action of phys and crys as modulators of the phot signal-output could be beneficial for a plant, allowing it to select forage areas with the highest photosynthetic light quality. One clear example of the interdependency, as well as complexity, of receptor systems regulating phototropism is illustrated by the responses of *phyA phyB* double mutants of Arabidopsis to unidirectional narrow-band BL. Under low to moderate fluences of BL etiolated *phyAphyB* seedlings exhibit < 5° total curvature, demonstrating that the magnitude of phototropic curvature under such conditions is almost completely determined by phy (Janoudi et al., 1997b), although phot1 is absolutely required for perception of the directional stimulus (Liscum and Briggs, 1995; Sakai et al., 2000). The story is complicated further under high fluence conditions, because *phyAphyB* seedlings retain a phototropic response largely equivalent in magnitude to that of wild-type (Janoudi et al., 1997b). Hence, under low fluence conditions phot1-activated processes dictate the direction of growth, while phyA and phyB determine the magnitude of the curvature response. In contrast, under high fluence conditions phot2 likely functions as the directional BL sensor (Sakai et al., 2001) and its activity, or that of another unidentified secondary receptor(s), determines the magnitude of the response. One can envision utilizing the natural variation that exists within the Arabidopsis germplasm as a tool to address this, as well as additional unresolved questions about phototropism.

The work done to date in Arabidopsis, and availability of mutants that disrupt various components of the phototropic response, provides an ideal system in which to examine the relationship between phototropism and fitness under natural, as well as experimentally modified, growth conditions. It is clear that many of the advances in our understanding of phototropism in the coming decade will require not only continued genetic, biochemical, and molecular approaches, but also their coupling to approaches aimed at addressing larger ecological and evolutionary questions – questions undoubtedly now more easily addressed because of the tools provided by genetic studies of phototropism in Arabidopsis.

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